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PEACE TIME BULLET WOUNDS OF THE ABDOMEN

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AND

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CHICAGO

This study, begun a number of years ago,[1] deals with the results of treatment in the Cook County Hospital, Chicago, of patients with bullet wounds of the abdomen (table 3) during the period from 1911 to 1924, when one of us (E. R. L.) made postmortem examinations in the morgue of that hospital for the coroner of Cook County. Although a decade has passed, it seems desirable to record these results. The number of patients, 343, is large; opportunity is given to compare the surgical work done in the period covered with that performed in the same hospital during subsequent years; the number of recoveries may be contrasted with those attained in other places, and, finally, because the theme is "peace time wounds" sustained in civil life, additional information is made available for reviewing the numerous differences between such wounds and wounds of the abdomen caused by missiles used in war.

The 343 patients who form the basis of this report were among a total of 432,293 patients admitted to the Cook County Hospital during the period covered by this study—a ratio of 1 to 1,260. During the year 1924 and during the period from 1911 to 1918, the only years available for comparison in our study, the ratio of patients entering the Cook County Hospital with bullet wounds of the abdomen was 1 to 1,692, whereas during the five years immediately following the World War, the ratio was 1 to 882. This disregard for human life exhibited during the years immediately following the war has been widely discussed.

Information as to the number of Negro patients in our series was obtained only from the records of the number of patients (205) who died and were examined at autopsy; this is not quite an adequate basis from which to draw conclusions. Of the 205 patients, 149 were white, 54 were Negroes and 2 were Mexicans. A number of surgeons in the

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1. Dr. W. M. Moncrief, Dr. Chester Guy, and Dr. G. J. Rukstinat assisted in examining some of the clinical records.

southern states have mentioned the greater resistance of Negroes in general to bullet wounds. But, as already stated, the absence from such records as now remain of information as to the number of Negro patients who recovered ends any further discussion of this matter. It is of interest, however, to know that tissues in the bodies of Negroes are more compactly knit together than those in the bodies of white persons and that in the postmortem examinations of the bodies of Negroes sharp knives are more quickly dulled.

STAGES IN THE DEVELOPMENT OF MODERN METHODS OF TREATMENT

A number of excellent accounts of the evolution of therapy of bullet wounds of the abdomen have been written.[2]

There was a long period before the discovery of anesthetics and antiseptic methods during which surgical procedures were inadequate. But there were many far-sighted surgeons during that time, especially those with military experience, who recognized that an ideal treatment would consist in opening the abdomen and repairing the injuries. Hamilton [3] carried this period back to statements made by Wiseman [4] in 1676, and the opinion of Wiseman was referred to in a later comment on the practice of treating gunshot wounds by surgical intervention.[5] But the subject was evidently not new then, as is apparent from the following quaint quotation by Otis [6] of advice given by Jherome of Bruynswyke,[7] who said in 1525:

> Whan the guttes is wounded ouertwhart or is in pecis, than it is dedly; yf it be lengthe woundyd, it may be holpen. If that the wounde of the belly is not grete

2. (*a*) Otis, G. A.: Injuries of the Abdomen, in Medical and Surgical History of the War of the Rebellion, Washington, D. C., Government Printing Office, 1877, part 2, vol. 2, chap. 6, p. 1. (*b*) Barnard, J. H.: Des plaies de l'intestin par armes à feu, Thèse de Paris, no. 263, Paris, A. Davy et Fils Ainé, 1887, p. 79. (*c*) Nimier, H.: Sur la séméiologie et le traitement des coups de feu de l'abdomen par petits projectiles, Arch. gén. de méd. **21**:207, 1888. (*d*) Verchère, F.: Des plaies de l'intestin par armes à feu de petit calibre, Rev. gén. d. sc. méd. **32**:297, 1888. (*e*) Amat, C.: Essai critique et clinique sur le traitement des lésions traumatiques de l'abdomen par projectiles de petit calibre, Gaz. méd. de Paris **1**:121, 1892. (*f*) Klemm, P.: Pathologie und Therapie der Schussverletzungen des Magens und Darms, Samml. klin. Vortr. no. 142, 1896 (Chir. no. 39, p. 321).

3. Hamilton, J. B.: Penetrating Pistol Shot Wound of Abdomen; Laparotomy; Suture of Intestine; Pelvic Hematoma; Recovery, J.A.M.A. **5**:202 (Aug. 22) 1885.

4. Wiseman, R.: Severall Chirurgicall Treatises, London, R. Royston, 1676.

5. Laparotomy in Gun-Shot Wounds of the Abdomen, editorial, J. A. M. A. **12**:54 (Jan. 12) 1889.

6. Otis, [2a] p. 116.

7. Brunschwig, H.: The Noble Experyence of the Vertuous Handy Warke of Surgeri, practysyd and compyled by the moost experte mayster Jherome of Bruynswyke, London, Peter Treverus, 1525.

inowgh, than shall ye make it greater as I shall shewe you hereafter, than shall you take out proply the guttes, and sow it thereafter as it is needful with a skynners nedyll. Jamericus, Theodoricus, Rogerius lay elder pypes in the guttes under the seme, that the same rotte not. Wilhelmus and some other, lay there in a part of a cryer of a throte goll of a beest, as the IV maysters sayth. But Lanfrancus and Guido they thinke it not be profytable, for that nature is inclyned to outdrawynge strange thyngys, and thus yt helpt not therefore it was layd, and it is better that the guttes be sowyd, as afore is sayd, and that it be clensyd of the unclenes.

Presumably similar opinions prevailed with regard to abdominal wounds before the days of firearms.

Many of these earlier surgeons did enlarge the wounds due to firearms and repair injuries apparent *de visu* et *de tactu*. Barnard [2b] mentioned twelve surgeons, beginning with Larrey in 1779, who treated wounds of the bowel in this manner. They did not perform laparotomies; abdomens were not opened freely and explored.[8] Barnard [2b] omitted from his list of twelve surgeons the name of Newell of New Brunswick, N. J., who told Sims [9] that he (Newell) had made "an incision 1½ inches above the crest of the ileum and removed a gun wad, composed of tow, paper, shot, a printer's type, and a piece of a man's vest—in all, sufficient to fill a tumbler half full." Recovery followed. This Newell did in 1847, the day after the shooting. His operation is included in MacCormac's table as a laparotomy, but the date of its execution was erroneously given by MacCormac as 1882, the year in which Sims announced that Newell had told him. Mention of Newell's operation is omitted from the list of laparotomies in the monograph by Martin and Hare.[10] Newell's patient had accidentally shot himself with a shotgun. Sims said: "Dr. Newell did, thirty-four years ago, what I now advise to be done in all cases of shot-wounds of the abdominal cavity." This is of interest solely with reference to who made the first laparotomy for bullet wounds. Kinloch [11] claimed he should be given the credit for this for an operation he performed on May 27, 1863. Others,[12] however,

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8. In some of the tables on laparotomies published subsequently, a few of these "débridement" operations are wrongly included, notably two by Baudens in 1830 and 1831, respectively, as stated by Otis,[2a] (p. 125) and by A. B. Graham, (Gunshot Wounds of the Abdomen, Indiana M. J. **20**:413, 1902), and one by Sevastopoulo as stated by Reclus (Bull. et mém. Soc. de chirurgiens de Paris **15**:132, 1889).

9. Sims, J. Marion: Remarks on the Treatment of Gunshot-Wounds of the Abdomen in Relation to Modern Peritoneal Surgery, Brit. M. J. **1**:184, 1882.

10. Martin, E., and Hare, H. A.: The Surgical Treatment of Wounds and Obstruction of the Intestines, Philadelphia, W. B. Saunders Company, 1891.

11. Kinloch, R. A.: Pistol-Shot Wound of the Abdomen Treated by Laparotomy and Suturing the Intestines, Tr. Am. S. A. **5**:183, 1887.

12. Stimson, L. A.: On Gunshot Wounds of the Abdomen with Especial Reference to Wounds of the Intestines, New York M. J. **50**:449, 1889.

have contended that this operation by Kinloch, performed seven months after the patient was shot, was done to repair a preternatural anus and was not a laparotomy.

The second period began with the demonstration that the abdomen may be opened widely with safety in order to search for and treat by surgical methods disease which it may contain. The declaration by Sims [9] in 1882, so often cited, that laparotomy for bullet wounds is as feasible as that for ovariotomy may have aided in making the procedure popular. But it should be remembered that when endorsement of such measures began, in about 1885, abdominal section for a great variety of diseases, mainly those of the female pelvic organs, had been widely practiced for some time. It had also been in vogue for the treatment of injuries of the abdominal organs due to causes other than firearms. Morton [13] credits Walter,[14] a well trained German surgeon who came to America at the suggestion of the surgeon Dieffenbach, with having performed the first laparotomy for intra-abdominal injury. The operation, which was successful, was done at Pittsburgh in 1859. Walter said: "Recovery from an injury of such a formidable character as rupture of the bladder with extravasation of urine into the abdominal cavity has not, as far as we know, ever been obtained by the ordinary means of practice." He insisted that his procedure was "not only legal but imperative." When Morton [13] made his first survey he found published or other information available about twenty laparotomies for stab wounds, nine for ruptured bladder and eight for lacerations of the bowel by blunt force. In view of the progress in abdominal surgery which had been made, it seems surprising that prompt laparotomy for bullet wounds of the abdomen was not advocated earlier.

This second period was brief, perhaps a decade or two. Ultimately a policy of prompt operation was fully sanctioned. But this required time, and for a number of years disputes in medical societies were quite general. Some surgeons were outspoken in expressing preference for noninterference; others were in favor of immediate laparotomy, and a third group advocated operation when certain symptoms appeared.[15] Amat [2e] enumerated twenty different meetings of the French society of surgery in Paris held from 1886 to 1891, at which these subjects were

13. Morton, T. S. K.: Abdominal Section for Traumatism, with Reports of Five Cases, J. A. M. A. **8**:225 (Feb. 26) 1887.

14. Walter, A. G.: A Case of Rupture of the Bladder Treated by Abdominal Section, M. & S. Reporter, Phila. **7**:153, 1861.

15. The surgical treatment of acute appendicitis underwent a similar evolution before surgical intervention followed the diagnosis as a routine as is the case at present, and controversies now prevail as to when removal of the acutely inflamed gallbladder is indicated.

debated. Reclus, who headed the noninterventionists, finally, in 1905,[16] announced his conversion to speedy laparotomy. Nancrede asked the members present at the meeting of the American Surgical Association in 1887 to express an opinion on the question "Should laparotomy be done for penetrating gunshot wounds of the abdomen involving the viscera?" [17] At the meeting of the New York State Medical Association in 1886 a symposium on shot wounds of the intestines was held, in which a number of conspicuous American surgeons took part.[18] This second epoch was also characterized by the publication of tables listing reports of laparotomies for abdominal bullet wounds almost as fast as they were announced. Table 1 shows the essential features of a number of such collections.

Comment on Table 1.—Morton claimed that the list of laparotomies published with his first article [13] was the first collective summary made and that MacCormac [19] included it as an appendix to his oration. In Barnard's thesis, which appeared the same year, there are two tables. All the tables put forth subsequently by different authors have as their nucleus the reports of laparotomies listed by MacCormac, supplemented by others to complete the number made to date. In a few, reference to the more obvious operations for débridement are omitted.

The operation performed by Pirogoff [20] found a place in several of these early compilations. It was not included by Morton in the table accompanying his first article. By Barnard it was classified as a débridement. But the patient was lost sight of a few days after the operation, and whether he died or recovered was not learned. Consequently, many who were interested in reporting the progress of events in tables which included Pirogoff's operation as a laparotomy were required to calculate the mortality rate on one less than the actual number of cases listed in their tables. A portion of the title of Barker's [21] article reads, "Continuation from Sir William MacCormac's List"; that list referred to

16. In discussing a report by Savariaud (Double plaie pénétrante de la grosse tubérosité de l'estomac. Plaie du foie par balle de revolver. Intervention. Guérison, Bull. et mém. Soc. de chirurgiens de Paris **31**:845, 1905) and referring to the inferior equipment of hospitals in France he said: "Mais maintenant il n'en est plus de même et depuis quinze ans je suis devenu interventionniste" (. . . but now it is different, and in the last fifteen years I have become an interventionist).

17. Tr. Am. S. A. **5**:155, 1887; Ann. Surg. **5**:455, 1887; J. A. M. A. **8**:607 (May 28) 1887.

18. Tr. New York State M. A. **3**:93, 1887; M. News **49**:601, 1886.

19. MacCormac, William: The Annual Oration on Abdominal Section for the Treatment of Intra-Peritoneal Injury, Brit. M. J. **1**:975 and 1031, 1887.

20. Pirogoff, N.: Grundzüge der allgemeinen Kriegschirurgie, Leipzig, F. C. W. Vogel, 1864, p. 578.

21. Barker, A. E. J.: Notes on Two Cases of Laparotomy for Penetrating Gunshot Wound of the Abdomen; Recovery in One, Brit. M. J. **1**:571, 1880.

thirty-two cases because MacCormac in the reprints of his oration added reports of two more laparotomies to that of the thirty he first collected.[22] To these Barker added reports of twenty-six.

TABLE 1.—*Early Statistics*

Author	Year	Total	Deaths	Mortality (Percentage)	Comment
Morton, T. S. K.: Abdominal Section for Traumatism, Proc. Philadelphia Co. M. Soc. **8**: 11, 1888 (read before the Society Jan. 26, 1887); Abdominal Section for Traumatism with Reports of Five Cases and Tables of All Recorded Cases, M. News **50**: 215, 1887; footnote 13	1887	22	17	77.2	18 of the 22 laparotomies were performed by American surgeons
Barnard [5b]	1887	24	18	75.0	Laparotomies were performed as follows: in 1882, 2; in 1883, 1; in 1885, 6; in 1886, 12; in 1887, 3
MacCormac [19]	1887	30	22	73.3	Morton's list of 22 is included
Carson, N. B.: Injuries of the Abdomen and Their Proper Treatment, J. A. M. A. **9**: 577 (Nov. 5) 1887	1887	44	30	68.4	MacCormac's table is included
Chauvel, J.: De la conduite à suivre dans les blessures par coup de feu des cavités viscérales, Cong. franc. de chir. Proc.-verb. **3**: 55, 1888	1888	41	29	70.7	All but 3 cases listed in MacCormac's table are included; in these 3 débridement operations were performed
Coley [6b]	1888	74	44	59.4	Of patients having laparotomies in the first 12 hrs., 17 recovered and 22 died
Dalton, H. C.: Gunshot Wound of the Stomach and Liver Treated by Laparotomy and Suture of Visceral Wounds with Recovery, Ann. Surg. **8**: 81, 1888	1888	69	41	59.4	MacCormac's list is included
Barker, E. E. J.[21]	1888	58	35	60.3	MacCormac's list is included
Morton, T. S. K.: Abdominal Section for Traumatism with Tables of Two Hundred and Thirty-Four Cases, J. A. M. A. **14**: 1 (Jan. 4) 1890.	1890	110	74	67.2	Sixty-eight American surgeons operated on 94 patients; 16 foreign surgeons operated on the remaining 16
Körte [23]	1890	64	42	65.6	Körte does not give a table; his material was derived mainly from American literature
Martin and Hare [10]	1891	120	86	66.2	Several "débridement" operations are included
Coley, W. B.: The Treatment of Penetrating Gunshot Wounds of the Abdomen, with an Analysis of One Hundred and Sixty-Five Cases Treated by Laparotomy, Am. J. M. Sc. **101**: 243, 1891	1891	165	111	67.0	This article includes a number of operations not mentioned in the literature
Lühe: Zur Behandlung durchbohrender Bauchwunden, Deutsche mil. ärztl. Ztschr. **21**: 145, 204 and 253, 1892	1892	152	95	62.5	The mortality (53 deaths) for 92 patients whose laparotomies were performed during the first 12 hrs. was 57.4%
Conner [20]	1893	188	127	67.5	Fifty-five American surgeons performed 174 laparotomies; there were 123 deaths

The title of Körte's article [23] intimates that his material was possibly derived from surgical experience in time of war, but it was obtained chiefly from American literature. MacCormac [19] said that gunshot

22. There are only thirty in the translation into German of his oration (Samml. klin. Vortr. no. 316, 1888 [Chir. no. 99, p. 3025]).

23. Körte, W.: Die Kriegschirurgische Bedeutung und Behandlung der Bauchschüsse, Berl. klin. Wchnschr. **27**:72, 1890.

wounds of the intestine are "far from being rare in civil practice, especially in America, where everyone carries a revolver and often uses it on small provocation." We have been unable to find many references to bullet wounds of the abdomen in the Italian literature. Apparently, stabbing was and has continued to be the more favored practice in Italy. The introduction of the use of laparotomy for bullet wounds was definitely an American contribution to surgery, notwithstanding the fact that the first recovery from such an operation was reported by Kocher.[24]

This practice was introduced more particularly by surgeons in the southern states, where shooting was especially frequent among both white persons and Negroes. Brown [25] said in 1898: "I have no doubt but that there have been several hundred gunshot wounds of the abdomen, probably a thousand, in the last ten or twelve years in Birmingham, Ala., and the surrounding districts." The Charity Hospital in New Orleans has been referred to as a laboratory for research on bullet wounds. During a single decade, from 1900 to 1910, more penetrating wounds of the abdomen, stab wounds and bullet wounds were observed there than were sustained by the American forces in the entire Spanish-American War.[26] Loria [27] said that 1,299 patients with bullet wounds of the abdomen were admitted in the years from 1900 to 1931 inclusive. In 1925 a committee on gunshot wounds of the abdomen was appointed at the aforementioned hospital;[28] Loria was secretary and Matas, chairman. The habit of promptly performing laparotomy as a routine in cases of bullet wound of the abdomen spread so rapidly that frequently the operation was successfully carried out under extremely adverse conditions, e. g., in cabins of Negroes, in box cars, on plantations remote from conveniences usually regarded as essential and without skilled help, etc. An extensive dissertation could readily be written about this single phase of the development of abdominal surgery.

Conner [29] found that 174 of the 188 laparotomies regarding which he was able to obtain information were performed by fifty-five American

24. Kocher, T.: Schusswunde des Magens mit rasch eintretenden peritonitischen und Collapserscheinungen. Laparotomie 3 Stunden nach der Verletzung; Magennaht, Heilung, Cor.-Bl. f. schweiz. Aerzte **13**:598, 1893.

25. Brown, G. S., in discussion on Grant, H. H.: The Practical Management of Bullet Wounds of the Abdominal Viscera, Tr. South. Surg. & Gynec. A. **11**:50, 1898.

26. Van Schaick, H. D.: Penetrating Wounds of the Abdomen, J. Florida M. A. **14**:33, 1927.

27. Loria, F. L.: The Influence of Hemorrhage in Abdominal Gunshot Injuries, Ann. Surg. **96**:169, 1932.

28. Loria, F. L.: (*a*) Visceral Injuries in Gunshot Wounds of the Abdomen, New Orleans M. & S. J. **80**:283, 1927; (*b*) Prognostic Factors in Abdominal Gunshot Wounds, ibid. **83**:393, 1930.

29. Conner, P. S.: Laparotomy in Cases of Gunshot Wounds of the Abdomen, Tr. Pan-Am. M. Congr. 1893, Washington, D. C., Government Printing Office, 1895, pt. 1, p. 691; abstr., J. A. M. A. **21**:431 (Sept. 16) 1893.

TABLE 2.—*Reports by Single Surgeons and From Particular Hospitals*

References	Number of Patients	Necropsies	Mortality (Percentage)	Comments
Barrow, D.: Four Cases of Gunshot Wound of the Abdomen Treated by Laparotomy, with Remarks, J. A. M. A. **12**: 833 (June 15) 1889; Gunshot Wounds of the Abdomen with Cases, ibid. **15**: 203 (Aug. 9) 1890. Barrow, D. W.: Gunshot Wounds of the Abdomen, Kentucky M. J. **16**: 243, 1918	19	1	26.3	D. Barrow and D. W. Barrow, father and son, worked at Lexington, Ky. The two reports by D. Barrow concerned 6, and that by D. W. Barrow, 13, patients; 4 of the 6 and only 1 of the 13 died; 13 were Negroes, 6 were white persons. Injury-operation interval was: for 1 patient 13 hrs.; for the 18 remaining 6 hrs. or less; for many less than 3 hrs. One patient recovered after D. W. Barrow repaired 17 perforations and resected parts of both colon and small bowel
von Bramann: Zur Behandlung der Schusswunden des Dünndarms und Mesenteriums mit Krankenvorstellung, Verhandl. d. deutsch. Gesellsch. f. Chir., 1889, p. 118. Wiemuth: Die Behandlung der Schussverletzungen, Arch. f. klin. Chir. **60**: 482, 1900. Loening, K.: Die Behandlung der Schussverletzungen des Abdomens, Inaug. Dissert., Halle-on-Saale, Kaemmerer & Co., 1902. Stieda: Ueber Schussverletzungen des Abdomens, München. med. Wchnschr. **53**: 673, 1906	12	6	50.0	From von Bramann's clinic in Halle-on-Saale, from 1889 to 1906 inclusive: 12 patients; 6 deaths; 1 patient whose injuries were reported by von Bramann recovered. Wiemuth reported 7 cases with 3 recoveries (the cases of 6 of the 7 presented by von Bramann to the German Surgical Society, 1893, were never published). Loening reported 3 cases with 1 recovery. Stieda reported 1 recovery. The average injury-operation interval for those recovering was 6 hours; fo those dying 21.3 hrs.; of 7 patients having injuries to a single viscus, 3 recovered; of 5 having injuries of two or more viscera, 3 recovered
Körte, W.: Uber die Chirurgie der Gallenwege und der Leber, Samml. klin. Vortr. n. f. no. 40. (Chir. no. 12, p. 243), 1892. von Haselberg, A.: Zur Casuistik der Schussverletzungen im Frieden, Inaug. Dissert., Berlin, G. Schade, 1893. Kroner, M.: Erfahrung über Friedensschussverletzungen, Arch. f. klin. Chir. **75**: 643, 1905	15	5	66.6	From Körte's urban clinic, Berlin, Germany, from 1890 to 1903 inclusive: Körte had 3 cases with 1 death; Haselberg, 3 with 3 deaths, and Kroner, 9 with 6 deaths; of 15 patients operated on by different surgeons 10 died. One patient with no visceral injury recovered; of 3 with injury to a single organ 2 recovered, and of 11 with injury to 2 or more organs only 2 recovered. Average injury-operation interval, 7 hrs.
Marks [23]	23	1	26.0	Reports from the St. Louis City Hospital, St. Louis, from 1892 to 1895: 20 males and 3 females. Average injury-operation interval for 20 patients, 4.33 hrs.; for 3 not stated. Six deaths. In 7 patients the small bowel alone was injured; in 3 it was injured together with other organs; the stomach alone was injured in 1; it was injured along with other organs in 6; the colon alone was wounded in 2
Miles, A. B.: Gunshot Wounds of the Intestines: Clinical Report of Thirteen Cases; Remarks on Diagnosis and Treatment, Tr. Am. S. A. **11**: 337, 1893	13	None mentioned	61.5	From the Charity Hospital, New Orleans: Nine patients died; 4 recovered; 7 were Negroes; 5 were white persons; 1 patient's color was not stated. One white man recovered after 16 perforations of the bowel were repaired; 1 who died had 20 perforations of the bowel from shotgun missiles
Winslow, R.: Gunshot Cases, Maryland M. J. **34**: 314, 1895-1896; in New Orleans M. & S. J. **23**: 463, 1895-1896; Gunshot Wounds of the Peritoneal Cavity and Contained Viscera, South. M. Rec. **26**: 129, 1896; Report of Eight Cases of Penetrating Gunshot Wounds of the Abdomen, with Injury to the Hollow Viscera, Ann. Surg. **28**: 487, 1898; Penetrating Wounds of the Abdomen, J. A. M. A. **63**: 1165 (Oct 3) 1914; Gunshot Wounds of the Intestines, Bull. Univ. Maryland School of Med. **1**: 66, 1916. Winslow, N.: Penetrating Abdominal Wounds, Surg., Gynec. & Obst. **34**: 617, 1922	34	3	52.9	From the Maryland University Hospital Clinic: In 5 different articles (from 1896 to 1916) R. Winslow dealt with the wounds of 11 patients; there were 5 deaths in his series. N. Winslow in 1922 treated 23 patients; 13 died. Summarized data for the 34 patients are as follows: 18 deaths and 16 recoveries; 14 white persons, 18 Negroes and 2 whose race was not stated; 27 males, 6 females and 1 whose sex was not stated; the youngest was 8 yrs.; 17 died of wounds of hollow viscera; 1 who recovered had 14 perforations of the small bowel with bird shot; the injury-operation interval in most cases was less than 4 hrs.; bullet wounds of the duodenum in 1 body and of the colon in 2 others were discovered post mortem
Parker, W. E.: Bullet Wounds of the Abdomen, Tr. South. S. & Gynec. A. **9**: 272, 1896	13	3	53.8	From the Charity Hospital in New Orleans: Seven patients died, 6 recovered; one of the 4 Negroes, a boy, aged 15, recovered after 11 perforations were repaired; 12 underwent operations shortly after injury; 1 who died had a second laparotomy

a second laparotomy

McRae, F. W.: Penetrating Wounds of the Abdomen with Report of Cases, Tr. South. S. & Gynec. A. **11**: 22, 1898; Penetrating Wounds of the Abdomen, with Report of Cases, Virginia M. Semi-Month. **4**: 73, 1899; in discussion on Rodman, W. L.: Gunshot Wounds of Cavities, J. A. M. A. **40**: 421 (Feb. 14) 1903; Penetrating Wounds of the Abdomen, New York M. J. **89**: 521, 1909	15	4	60.6	From the Grady Hospital, Atlanta, Ga., from 1898 to 1908: The first 2 of the 4 articles are almost identical. Altogether McRae reported on laparotomies on 15 patients; the results were as follows: 10 deaths and 5 recoveries; 6 Negroes, 4 white persons and 5 whose race was not stated. The injury-operation interval was short, as a rule; of the patients who recovered 1 had wounds of only the stomach, 3 of only the ileum, 1 of only the liver and 1 of only the urinary bladder and ileum; in 1 body an overlooked wound of the colon was found post mortem
Oliver, J. C.: Fifty-Eight Cases of Gunshot Wounds of the Abdomen, Lancet-Clinic **40**: 463, 1898. Caldwell, C. E.: Penetrating Wounds of the Abdomen, with Report of Cases, Including a Case of Traumatic Rupture of Congenital Cystic Kidney, Tr. South. S. & Gynec. A. **18**: 398, 1906	26	14	69.2	From the Cincinnati General Hospital, Cincinnati: Oliver's report deals with laparotomies performed by himself and 4 other surgeons for penetrating bullet wounds of the abdomen in 22 patients. Caldwell deals with 4 patients. Comments are also made in each report on 1 case of a nonpenetrating bullet wound of the abdomen. Seventeen of the 26 patients died; overlooked wounds were found in 8 of the 14 bodies examined after death; Caldwell reported 1 death and 3 recoveries
Vaughan, G. T.: Gunshot Wounds of the Abdomen; Ten Intestinal and Twelve Perforations of the Mesentery; Operation, Recovery, M. News **73**: 113, 1898; Gunshot Wounds of the Ureter; Two Cases of Ureterovesical Anastomosis, Am. J. M. Sc. **129**: 449, 1905; Gunshot Wounds of the Abdomen; a Review of Fourteen Cases with Remarks on the Mortality and Treatment, Am. J. M. Sc. **131**: 285, 1906; Further Remarks on the Care of Gun-Shot Wounds of the Abdomen, with Especial Reference to the Treatment of Wounds of the Urinary Bladder and the Danger of Abscess and Fistula Following Wounds of the Pancreas, Am. J. M. Sc. **134**: 206, 1907	17	1	58.8	Report on surgical experiences in Washington D. C., from 1898 to 1907: 17 patients, 9 of whom died; 1 had multiple perforations of the ileum and a resection followed by death; another who died had a bruised bowel and hemorrhage from a wound made by a blank cartridge; a third recovered from a bullet perforation of 1 ureter; the remaining 14 had wounds of 2 or more viscera
Simons, M.: Gunshot Wound of the Abdomen, Tr. South. S. & Gynec. A., **12**: 45 and 203, 1900	20	None mentioned	85.0	Report by Simons, professor of surgery at Charleston, S. C.: There were 20 cases with 17 deaths; 1 patient with 15 holes of the small bowel, 1 with 2 ft. (60.96 cm.) of the small bowel resected and a third with 2 holes in the stomach recovered; many of the 20 patients were Negroes and were transported long distances. The average injury-operation interval was about 20 hrs.
Nietert, H. L.: Report of a Case of Gunshot Wound of Pregnant Uterus and Fetus: Cesarean Section; Recovery, M. Rev. **41**: 305, 1900; Penetrating Wounds of the Abdomen, Interstate M. J. **9**: 599, 1902	17	0	58.8	From the City Hospital, St. Louis: Data are given on 17 patients, 7 of whom recovered and 10 died, 7 dying of hemorrhage and shock during or immediately after operation; a woman 7 months pregnant recovered from a wound of the uterus and cesarean section; the fetus had a wounded shoulder and died of prematurity; necropsies are not mentioned
Tantzscher, K.: Zur Behandlung der perforierenden Bauchwunden, Samml. klin. Vorträge, n. f., Leipzig, no. 319 (Chir. no. 91, p. 247) 1901. Brehm, O.: Resultate bei den penetrierenden Bauchverletzungen des Friedens, Arch. f. klin. Chir. **73**: 234, 1904. Michelsson, F.: Zur Diagnose und Therapie der Schussverletzungen der Milz, Deutsche Ztschr. f. Chir. **124**: 328, 1913	20	1	35.0	From A. von Bergmann's clinic at Riga, Latvia: Tantzscher had 8 cases with 4 deaths; Brehm had 7 with 2 deaths; Michelsson had 5 with 1 death. One of Brehm's patients who recovered had wounds of the liver, stomach, spleen and splenic artery and underwent a splenectomy. The causes of death were as follows: wounds of the colon, 4; wounded spleen and peritonitis, 1; wounded liver, 1, and peritonitis without visceral injury, 1
Summers, J. E.: Personal Experiences with Contused Gunshot and Stab Wounds, West. M. Rec. **7**: 107, 1902	10	0	70.0	From private practice in Omaha: Reports are given of 7 deaths, 5 from hemorrhage and 2 from peritonitis. Of the patients who recovered, 1 had no viscus injured, 1 had a wounded kidney, and 1 had wounds of 1 lung, the liver and spleen

TABLE 2.—*Reports by Single Surgeons and from Particular Hospitals—Continued*

References	Number of Patients	Necropsies	Mortality (Percentage)	Comment
Brown, J. Y.: Penetrating and Perforating Gunshot and Stab Wounds of the Abdomen with Reports of Cases, Am. J. Obst. **48**: 707, 1903; New York M. J. **70**: 726, 1904; Report of Case, Penetrating Gunshot Wound of the Abdomen, Louisville Month. J. M. & Surg. **11**: 346, 1904-1905; St. Louis M. Rev. **51**: 254, 1905	10	2	50.0	From the City Hospital, St. Louis: Each of the 2 articles appeared in 2 different journals. Observations on 10 patients are discussed. There were 8 male and 2 female patients; 5 of the male, and none of the female patients died. For 7 the injury-operation interval was short; 4 of the 5 who died had resections of the bowel; the other who died had a bleeding wound of the liver; an overlooked wound of the cecum was found post mortem in 1 body
Ossig: Zur Pathologie und Therapie der Revolverschussverletzungen des Kopfes und Rumpfes, Beitr. z. klin. Chir. **37**: 511, 1903. Tietze: Magenschuss, Centralbl. f. Chir. **36**: 312, 1909. Scheyer, K.: Uber Nierenschussverletzungen, Klin. Wchnschr. **1**: 1459, 1909	10	2	60.0	From Tietze's surgical clinic at Allerheiligen Hospital in Breslau, Germany: A total of 10 cases with 6 deaths are reported. Ossig had 5 with 4 deaths; Tietze 3 with no deaths; Scheyer had 2 with 2 deaths. Of 5 patients with injury to a single organ, only 1 died; all with injuries to 2 or more organs died; in 1 body a wound of the stomach, and in another an extraperitoneal wound of the urinary bladder were overlooked. The injury-operation interval is stated for 2 patients only; for 1 it is given as "prompt," for the other as a "few hours"
Gebele, H.: Ueber penetrierende Bauch-Stich-und Schusswunden, München. med. Wchnschr. **50**: 1415, 1903	15	None mentioned	46.7	From Angerer's surgical clinic in Munich, Germany, from 1897 to 1902: Seven of the 15 patients reported on died
Harris, M. L.: On the Treatment of Penetrating Wounds of the Abdomen, Ann. Surg. **39**: 356, 1904	10	3	30.0	From various hospitals in Chicago: Three of 10 patients died. In 1 body there were found after death 2 holes in the stomach and 1 wound of the diaphragm which had been unsuspected at the time of the operation. The injury-operation interval was 5 hrs. or less; in 2 patients who recovered no viscus was injured
Oppel, W. A.: Uncomplicated Compound Gunshot Wounds of the Stomach, Russk. vrach. **3**: 1177, 1904; Beobachtungen über Schussverletzungen der Bauchhöhle in Friedenszeit, Arbeiten der propädeutischen chirurgischen Klinik. von W. A. Oppel, 1910, vol. 1; abstr., Centralbl. f. Chir. **38**: 514, 1911	11	1	36.3	From the Surgical Clinics of Prof. Lederoff and W. A. Oppel, Military Medical Academy: Of 11 patients, 7 recovered and 4 died; the injury-operation interval was 1 hr. for 9, 3 hrs. for 1 and 7 hrs. for another, the last 2 patients both dying; in 1 who recovered, the bullet entered the stomach and later passed by way of the bowel
Froloff, V. I.: Diagnosis and Treatment of Penetrating Wounds of the Abdominal Cavity in Time of Peace, Voyenno-med. J. (med.-spec. pt.) **215**: 35, 249 and 459, 1906	13	4	46.1	From the Municipal Hospital, Batum, Russia: Reports are given on 11 male and 2 female patients; the youngest was 13, the oldest 50; 7 patients recovered and 6 died; of those recovering, 5 had only wounds of the intestines, 1 had only a wound of the liver and 1 had no visceral injury; of those dying, 5 had wounds of the stomach only and 1 had wounds of the colon only. The injury-operation interval was stated to be from "immediately" to 24 hrs. after injury. In one patient an overlooked wound of the gallbladder was found post mortem
Imbert, L.: Etude du pronostic dans les laparotomies pour plaies pénétrantes de l'abdomen, Cong. franç. de Chir. Proc.-verb. **20**: 259, 1907	17	Some made	76.4	From Marseilles, France: Seventeen patients had bullet wounds; 13 died and 35 had laparotomies, but injuries due to stabbing and those due to shooting are for the most part discussed indiscriminately
von Hofmann, A.: Ueber Friedensschussverletzungen, Beitr. z. klin. Chir. **53**: 778, 1907	11	0	55.5	From Beck's clinic in Karlsruhe, Germany, from 1897 to 1907: Six patients died, 1 dying of tetanus 10 days after the injury

Bestelmeyer, R.: Ueber Schussverletzungen, Beitr. z. klin. Chir. **55**:637, 1907	17	9	53.0	From the Angerer Clinic of Munich, Germany, from 1897 to 1907: Of 9 patients who died, 3 entered moribund. In 1 body a wound of the duodenum, and in another a wound of the left lung, was undiscovered at the operation
Riebel, E. C.: Abdominal Gunshots, Surg., Gynec. & Obst. **4**:202, 1907	26	6	34.6	From Chicago: At the Provident Hospital 11 patients underwent laparotomies; at the People's Hospital, 15. Dr. W. E. Schroeder operated on 16; Dr. Riebel, on 9; for 1 the surgeon is not named. There were 25 males and 1 female; 15 Negroes and 11 white patients. Nine patients died. Of 9 with thoraco-abdominal wounds, 4 recovered; 3 of 4 patients with resections of the bowel recovered; 1 recovered after splenectomy and nephrectomy
Després, J.: Vingt cas de plaies pénétrantes par balles de revolver; crâne; thorax; abdomen; rachis, Cong. franç. de chir. Procès verb., mém. et disc. **21**:952, 1908	20	7	40.0	Report on surgical work by Després at Toulon, France, from 1900 to 1908: Eight patients died: 4 of wounds limited to the stomach; 1 of wounds limited to the omentum, 1 of wounds limited to the liver and 1 of injuries limited to the right kidney. Recoveries occurred; no details of necropsies are given
Hagentorn, J. A.: Ueber Bauchschüsse im Frieden und ihre Behandlung, Deutsche Ztschr. f. Chir. **92**:1, 1908; Ueber Schussverletzungen im Frieden, ibid. **128**:433, 1914 **128**:433, 1914	14	0	78.5	From the Municipal Hospital, Kwono, Russia: Several surgeons performed operations; 11 of the 14 patients died, 1 of wounds made by a toy cannon; 1 recovered from wounds made by two bullets fired into the abdomen
Graham, C.: Gunshot Wounds of the Abdomen: A Report of Nine Cases; Seven Penetrating Wounds of the Viscera and Two Non-Penetrating, Surg. Gynec. & Obst. **8**:354, 1909; Gunshot Wounds of the Intestines, Kentucky, M. J. **11**:209, 1912-1913	14	2 mentioned	35.7	From Graham's private practice in Henderson, Ky.: Twelve of the 14 patients were shot in front; 2 were shot from behind; in 2 of the 5 who died no abdominal viscus was injured; 1 had wounds of only the small bowel; 1 had wounds of both large and small bowel (39 perforations in the latter); 1 had wounds of the stomach, colon and small bowel. There were 11 male and 3 female patients
Okinschewitsch, A. J.: Penetrierende Stich- und Schusswunden des Bauches nach den Erfahrungen des Krankenhauses in Balakhany-Sabuntshi von 1905 bis Mitte 1908, Baku, 1909; abstr., Centralbl. f. Chir. **37**:583, 1910	21	0	66.6	From the hospital in Balakhany-Sabuntshi, U. S. S. R., maintained by industries for the preparation of naphtha employing Russians, Persians, Armenians, etc.: Of the 7 patients who recovered, 3 had no visceral injuries, 3 had injuries of the stomach, and 1 had an injury of the colon; of those who died, 10 had wounds of the small bowel only, 2 of the colon only, 1 of the liver only and 1 of the colon and small bowel. The injury-operation intervals and necropsies are not mentioned
Branch, J. B. B.: Penetrating Wounds of the Abdomen, Ann. Surg. **54**:164, 1911	15	None mentioned	53.3	From the Macon Hospital, Macon, Ga., from 1909 to 1910: Six different surgeons performed operations; 8 patients died, 2 dying on the table; 7 recovered. There were 14 males and 1 female; 13 Negroes and 2 white patients. Two patients who recovered had no abdominal viscus wounded; the average injury-operation interval for the patients who recovered was 3.75 hrs.; for those who died, 7.25 hrs.
Besley, F. A., and James, W. A.: The Time Element in the Operative Treatment of Abdominal Injuries, with a Consideration of 172 Cases Taken from the Records of Cook County Hospital, Illinois M. J. **25**:87, 1914	43	No details	51.0	From the Cook County Hospital, Chicago: A number of surgeons performed operations; 22 of the 43 patients died
Crawford, L. B.: Gunshot Wounds of the Abdomen, Statistics from Charity Hospital, 1906-1913, and Reports of Two Cases Operated On, New Orleans M. & S. J. **67**:1, 1914	52	0	61.0	From the Charity Hospital, New Orleans, from 1906 to 1913: A number of surgeons performed operations; 32 of the 52 patients who had laparotomies died
Camaggio [60]	117	0	61.5	From the Pellegrini Hospital in Naples, Italy, from 1901 to 1914: Two hundred and sixty-eight patients were treated for bullet and 1,225 for stab wounds of the abdomen; 19 had injuries from blunt force. Consideration of the different types of injury by Camaggio is impartial and casual. One hundred and seventy-seven of the patients wounded by bullets had laparotomies; 70 recovered. No information about necropsy or the injury-operation interval is given

TABLE 2.—*Reports by Single Surgeons and from Particular Hospitals—Continued*

References	Number of Patients	Necropsies	Mortality (Percentage)	Comments
Hays, G. L.: Gunshot Wounds of the Abdominal Cavity, with Report of Cases, Surg., Gynec. & Obst. **22**: 176, 1916	18	0	38.8	From the Mercy Hospital, Pittsburgh: Seven of the 18 patients died. The average injury-operation interval was about 9 hrs.; for those who died it was about 6 hrs.; for those who recovered it was about 4.4 hrs.
Goltman [64]	42	2	73.8	From the General Hospital, Memphis, Tenn.: Fourteen surgeons performed operations. Data are given on 42 patients who underwent operations; 31 died
Smital, W.: Ueber Stich- und Schussverletzungen des Bauches, Wien. med. Wchnschr. **70**: 653, 1258, 1306, 1442, 1502, 1547 and 1602, 1920. Finsterer, H.: Zur Diagnose und Therapie der Leberverletzungen, Beitr. z. klin. Chir. **119**: 598, 1920	18	3	33.3	From Hochenegg's clinic in Vienna, from 1900 to 1920: Smital reports the occurrence of wounds of only hollow viscera in 8, of only solid viscera in 2 and of wounds of both types in 2 patients. Twelve patients recovered; 5 died; all the patients were males; the average age was 25½ yrs. Overlooked wounds of the right lung, liver and diaphragm were found in 1 body. For the patients who recovered, the average injury-operation interval was 5.4 hrs., for those who died it was 12 hrs. Finsterer adds a report of 1 case in which a wound of the liver and one of the colon caused death
Kleinschmidt, O.: Ueber Bauchschuss und Schock, Arch. f. klin. Chir. **117**: 569, 1921	22	8	63.6	From political riots in Leipzig, Germany: Fourteen of the 22 patients who had laparotomies died; 3 others entered moribund and died without operations. The 22 laparotomies were performed within 3 hrs. after injury; 9 patients were between 9 and 18 yrs. old.; 10 deaths were attributed to bleeding; wounds of one ureter in 1 body, of the colon in a second, of the small bowel in a third, overlooked at the time of operation, were found post mortem
Farmer, C.: Gunshot Wounds of the Abdomen: Report of Cases, Kentucky M. J. **19**: 591, 1921; Gunshot Wound of Abdomen Followed by Subphrenic Abscesses: Continued Report, Kentucky M. J. **20**: 104, 1922	13	One mentioned	69.2	From the City Hospital, Louisville, Ky.: Eight surgeons performed operations; 9 of the 13 patients died; the average injury-operation interval was about 4 hrs. Detailed protocols are given for only 7 patients. One reported on in 1921 as having recovered died (see Farmer's second article) of an overlooked perforation of the back wall of the stomach and a subphrenic abscess
Prat, D.: Heridas del abdomen por arma de fuega, An. de Fac. d. med., Montevideo **6**: 455 (July) 1921	15	1	40.0	From Montevideo, Uruguay: Five patients died of solely abdominal and 1 of thoraco-abdominal wounds. In the single necropsy mentioned, an overlooked wound of the colon was found; a woman recovered after 6 holes in the bowel and 4 in the mesentery were repaired; a man who recovered had 16 perforations in the small bowel and 1 in the mesentery
Vale [52]	80	0	44.0	From the Receiving Hospital, Detroit, from 1920 to 1923: There were 67 male and 13 female patients; 30 Negroes and 50 white patients; 35 died; 9 deaths occurred in the operating room; there were multivisceral wounds in 50, a wound of a single viscus in 26 and no viscera injured in 4 cases
Condiet, W. L.: Perforated Gunshot and Stab Wounds of the Abdomen, Ann. Surg. **80**: 51, 1924	19	1	45.0	From the Gouverneur Hospital, New York, from 1911 to 1922: Operations were performed by different surgeons; 16 were on men, 2 on women and 1 on a patient whose sex was not stated. Eight patients recovered; 1 of these had 8 perforations of the bowel and 6 inches (15.24 cm.) of the bowel was resected (Murphy button)

Hauser, C. D.: Traumatic Perforations of Abdominal Viscera, Ohio State M. J. **21**: 162, 1925	17	0	23.5	Report on surgical work by Hauser and his colleagues in Youngstown, Ohio: Data are given on 17 patients; 4 died and 13 recovered; 2 pregnant women had wounded uteri; in 1 the fetus was killed by a bullet; the other underwent a cesarean section; the delivered child and both women recovered; 7 patients who recovered had multiple perforations of the bowel as follows: 14, 8, 8, 7, 6, 6 and 4; 2 died and 1 recovered after splenectomies
Davis, M. B.: Gun Shot and Stab Wounds of the Abdomen: An Observation of Twenty-Eight Cases and the Immediate End Results, J. Tennessee M. A. **18**: 190, 1925	20	0	65.0	Report on surgical work by Davis in Nashville, Tenn. Four of the 13 deaths were from thoraco-abdominal wounds
Steckbauer, J. W.: Gun Shot Wounds of the Abdomen in Civil Life, Wisconsin M. J. **25**: 179, 1926	26	14	53.8	From the St. Louis City Hospital, St. Louis: Steckbauer performed laparotomies on 26 patients; 12 recovered and 14 died, 11 of peritonitis and 3 of shock. There were 22 male and 4 female patients; 15 were white persons and 11 were Negroes. The injury-operation interval and the dates of the operations are not stated; in 2 bodies overlooked perforations were found after death; the location was not stated
Bivings, C.: Treatment of Gunshot Wounds of the Abdomen, J. M. A. Georgia **16**: 166, 1927	66	0	60.6	From the Grady Hospital, Atlanta, Ga.: Data are given on the work of various surgeons; 40 of the 66 patients died, 8 dying from 1 to 7 hours after admission
Loria [35]	76	0	61.8	From the Charity Hospital, New Orleans: Forty-seven patients died and 29 recovered; the injury-operation interval in most cases was 2 hours or less; in reference 35*b* factors influencing the prognosis in this series are discussed
Miller, M. O.: Gunshot Wounds of the Abdomen, New Orleans M. & S. J. **80**: 279, 1927	46	0	56.5	From the Charity Hospital, New Orleans, from July 1, 1925 to June 13, 1927: Twenty-six patients died; 31 of the 46 patients were Negroes, 38 being male and 8, female
McKeithen, A. M.: Penetrating Wounds of the Abdomen: a Study of Sixty-Nine Cases, Kentucky, M. J. **27**: 77, 1929	56	0	44.6	From the City Hospital, Louisville, Ky.: Twenty five patients died
Billings and Walkling [31]	114	50	48.2	From the Pennsylvania Hospital, Philadelphia, from 1909 to 1930: Fifty-five of the 114 patients died. In 11 of the 50 necropsies, overlooked wounds were found; in 6 of the 11 bodies there were such overlooked wounds of 2 or more organs, and in the remaining 5 bodies wounds of a single organ were overlooked
Willis [42]	58	0	25.8	Report on surgical work at Rocky Mount, N. C.: About five sixths of the patients were Negroes; 15 died. The wounds in 10 were made with the missiles from shotguns; 4 patients recovered
Oddone, G. S.: Consideraciones sobre 38 casos de abdomen agudo traumatico con lesión de visceras huecas: Resultado operatorio, Bol. y trab. de la Soc. de cir. de Buenos Aires **17**: 367, 1933	16	0	31.0	Oddone worked in Cordoba, a province of Argentina; 5 patients died
Prey, D., and Foster, J. M.: Gunshot Wounds of the Abdomen, Ann. Surg. **99**: 265, 1934	22	0	72.7	From the Denver General Hospital, Denver: Fifteen of the 22 patients died. For those who recovered, the average injury-operation interval was 1.88 hrs.; for those who died it was 3.4 hrs.
Oberhelman and LeCount	301	169	61.5	From the Cook County Hospital, Chicago, from 1911 to 1924: One hundred and eighty-six patients died; 37 surgeons performed operations

surgeons and that 123 deaths resulted. In the much smaller group in Morton's first collection, 18 of the 22 operations were performed in this country. Following the successful operations by Kocher,[24] Bull [30] and Hamilton [3] the expediency of performing laparotomies for bullet wounds of the abdomen was quickly recognized, and the practice was adopted in America. The number of such operations soon became too large to be recorded in tables, and the publication of such tables gradually ceased. In the preface to their monograph Martin and Hare wrote: "We have collected and placed before the reader what we believe to be the fullest statistics yet collected upon gunshot wounds of the abdomen." Their work was awarded the Fiske Fund Prize on July 12, 1890. They did not state when their manuscript was finished.

Many authors have commented on the unreliability of the mortality rates contained in the early literature on laparotomies for bullet wounds of the abdomen.[31] This is based, of course, on the disposition to report only the successful operations. In order to lessen this error, Conner [29] obtained his figures from answers to a questionnaire sent to prominent American surgeons. Replies came from seventy-three, of whom eighteen had never performed operations for bullet wounds of the abdomen. He asked that the whole number of laparotomies performed by each surgeon as well as the number in which recovery occurred be given.

Publication of the accomplishments of single surgeons or the experiences at particular hospitals marks the third period in the recital of conspicuous stages of the development of modern methods of treatment of bullet wounds of the abdomen. We are now in this epoch which is well along toward completion. The evolution of any special improvement in surgery is apparently marked by similar features: a time when the demand for a new operative treatment is a matter of common agreement but methods are still undevised; a period marked by announcements in "case reports" that the difficulties are overcome; collection and publication in tables of successful operations of the type under consideration; the third period, already defined, ending when mortality rates are fairly stable and reports published by single surgeons of their results with large numbers of the new operation no longer command the attention they formerly received. Table 2 deals with this third period.

DATA COMPARABLE WITH THOSE FROM THE COOK COUNTY HOSPITAL

Comment on Table 2.—Table 2 is based on what data we have been able to find in the literature suitable for comparison with the products of our examination of the records of the work done at the Cook County

30. Bull, W. T.: A Case of Gunshot Wound of the Intestines Treated Successfully by Laparotomy with Suture of the Intestines, M. News **46**:171, 1885.

31. The comment of Imbert (Étude du pronostic dans les laparotomies pour plaies pénétrantes de l'abdomen, Cong. franç. de chir. **20**:259, 1907) is particularly just and thoughtful.

Hospital. We have arbitrarily included in this table only such reports as are concerned with laparotomies for penetrating bullet wounds of the abdomen performed on at least 10 patients by one or more surgeons in the same hospital or by one surgeon at different places. Laparotomies for nonpenetrating bullet wounds of the abdomen are not included. Unless strictly intra-abdominal structures or viscera were also injured we have also aimed to exclude wounds of the kidneys, ureters and extraperitoneal portions of the rectum and bladder. Laparotomies for wounds made by bullets passing through the abdomen and kidneys, ureters or large blood vessels are included even though intra-abdominal viscera escaped injury. The facts presented by many writers we have been unable to use because they have considered bullet wounds and stab wounds undiscriminatingly. In some articles the statistics set forth in the text differed from those in the tables. In order to maintain uniformity, we have been compelled to make new calculations for mortality rates because the writers included the deaths of patients who died without operations with those of patients who died after laparotomies. Our study is definitely one of mortality rates *after* laparotomies. When an author reported additional experiences with bullet wounds of the abdomen in one or more subsequent articles, as did Hagentorn, for example, these reports are given a single place in the table.

The observations of D. Barrow and D. W. Barrow, father and son, of Lexington, Ky., are considered together, notwithstanding the lapse of time between them and the presumably improved surgical methods. The remarks apply to R. Winslow and W. Winslow of Baltimore. The bullet wounds of the abdomen sustained during street rioting in Leipzig and reported by Kleinschmidt are included in the table. They may be regarded as borderline injuries midway between wounds sustained in peace time and those sustained in war, but they were not from shrapnel or other missiles the use of which is peculiar to war. In many respects the wounds sustained in street fights, especially those from rifles, are like those sustained in war.[32] Street fights also occurred in Chicago during the race riots of July and August 1919, but only 1 victim of these riots with a bullet wound of the abdomen was received at the Cook County Hospital. This was a white man who died without an operation.

It is quite possible that overlapping occurs in the reports from some hospitals, different authors including accounts of the same patients. For example, Gebele's account is based on bullet wounds of the abdomen cared for in Angerer's clinic in Munich from 1897 to 1902, and that of Bestelmeyer deals with reports from the same clinic for the years

32. Meixner, Karl: Schussverletzungen durch Handfeuerwaffen, Arch. f. Kriminol. **75**:91, 1923. De, J. C.: A Medicolegal Study of the Calcutta Riots of 1926, Indian M. Gaz. **62**:479 (Sept.) 1927. Meixner, K., and Werkgartner, A.: Schussverletzungen im Strassenkampf, Beitr. z. gerichtl. Med. **7**:32, 1928.

from 1897 to 1907. In the inaugural dissertation by Angerer [33] there are accounts of laparotomies performed in that clinic for bullet wounds on 4 patients in 1897 and on 1 in 1901. These cases are probably also reviewed in the article by Gebele and in that by Bestelmeyer or in both. A similar statement applies to two cases in which treatment given at that clinic in 1901 and 1904 is described by Riester.[34] Observations in the St. Louis City Hospital, recorded by Marks, Nietert and Brown, each of whom gave data for a different period, presumably pertain to different patients, but Steckbauer, whose article appeared much later, failed to state when he performed laparotomies for bullet wounds of the abdomen on 26 patients in the aforementioned hospital. Some of the 43 cases of laparotomy for such wounds mentioned by Besley and James are probably included in our series. They covered all varieties of penetrating wounds of the abdomen, and those due to bullets received less consideration than those caused in other ways. The report of one of the patients cared for by Straus [35] is included in our series. Richter [36] mentioned the cases of 8 children with bullet wounds of the abdomen cared for in the Cook County Hospital. Two of these 8 cases are included in our series; in both recovery occurred. A third case in our series is included in the report by Levin,[37] whose article is based on Richter's material as well as on additional observations made at both the Mount Sinai Hospital and the Cook County Hospital in Chicago. The third child also recovered. All 3 children had laparotomies. Levin failed to state when the observations he reported were made. They probably concern a period subsequent to that covered by our series. The reports from von Bergmann's clinic by Tantzscher, Brehm and Michelsson deal with patients cared for at that clinic from 1904 to 1908. The fourth report is by Jankowski.[38] He, unfortunately, failed to indicate the mortality rate for bullet wounds separately from that due to other causes. Consequently his information cannot be included with that contained in the reports by Tantzscher, Brehm and Michelsson. Michelsson's study was limited to bullet wounds of the spleen as observed in the clinic at Riga, Latvia, during the period from 1890 to 1912. He found that 10 patients had been treated for such injuries, but only 6 of the 10 had undergone laparotomies. Brehm had previously described the injuries in 1 of those

33. Angerer, T.: Ueber Stich- und Schussverletzungen des Magens, Munich, Kastner & Callny, 1903.

34. Riester, H.: Milzexstirpation nach Schussverletzung, Würzburg, J. Meixner, 1912.

35. Straus, D. C.: Recent Gunshot Wounds of the Kidney with Report of Four Cases, S. Clin. North America **2**:635, 1922.

36. Richter, H. M., in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 3, p. 485.

37. Levin, I. M.: Abdominal Injuries in Children, Ann. Surg. **87**:718, 1928.

38. Jankowski, J. J.: Ueber penetrierende Stich- und Schusswunden des Bauches, Inaug. Dissert., Riga, 1909 (Russisch), Centralbl. f. Chir. **37**:581, 1910.

6 patients, and Jankowski had described those in 3. The other 2 cases were first mentioned in Michelsson's article.

The common use in New Orleans of pistols and revolvers as weapons has led to more contributions from the Charity Hospital in that city than from any other single institution. Five authors, Miles, Parker, Crawford, Loria and Miller, who worked in New Orleans, are mentioned in table 2. Duplication by these authors, however, is probably only in the reviews of Loria and Miller, as they cover the same period: from 1925 to 1928. Fenner's [39] summary, however, includes stab and bullet wounds of the abdomen treated at the Charity Hospital during the period from 1892 to 1901. Presumably his contribution embraces observations previously set forth by Miles in 1893 and by Parker in 1896. It is quite likely that further search would disclose reports from single clinics or hospitals [40] by several writers so that other groups of 10 or more cases could be added to table 2.

The total number of patients with bullet wounds of the abdomen with laparotomy collected from the literature in table 2 is 1,494; 789 of the patients died—a mortality rate of 52.8 per cent. The contributions in this table are arranged chronologically. Those published during the years covered by our series deal with 535 patients, of whom 300 died—a mortality rate of 56 per cent—as compared to 301 patients with 185 deaths—a mortality rate of 61.4 per cent—in our series. Concerning our own series we present the following comments as well as tables 3 to 18. In some of the tables there is overlapping, and this is explained in the footnotes to some of them, for example, in the footnote to table 6.

COOK COUNTY HOSPITAL SERIES

General Considerations (Tables 3, 4 and 5).—The wounds were such as are usually produced by homicidal, suicidal and accidental shootings occurring in large cities. None of the 343 patients was wounded with the kind of machine-guns now used by gangsters. Strictly speaking, wounds due to the small lead pellets used in shotguns to shoot ducks and other wild game ought not to be included with bullet wounds of the abdomen. But following a practice set by other writers we have included the single shooting of this character with the other 342 occurring in the period covered by the series. The case was that of a man, aged 23, who was shot in a fight in a saloon. A huge gaping laparotomy

39. Fenner, E. D.: Report of Six Cases of Penetrating Wounds of the Abdomen Submitted to Abdominal Section with a Statistical Table of One Hundred and Fifty-Two Cases Thus Operated on at the Charity Hospital in New Orleans, La., Ann. Surg. **35**:15, 1902.

40. Such a search yielded the information regarding the 12 patients treated in von Bramann's clinic in Halle, Germany, reported by different authors over seventeen years. (See the second item in table 2.)

wound with protruding gangrenous loops of small bowel was found at the postmortem examination; the interval between the injury and the operation was seventeen hours; forty-three small perforations in the small bowel were repaired; death occurred two weeks after entrance to the hospital and resulted from peritonitis and sepsis with multiple small pulmonary embolic abscesses.

The mortality from shotgun wounds is high. Many of the victims are shot at close range. Bunch,[41] of Columbia, S. C., had 7 patients

TABLE 3.—*The Cook County Hospital Series*

Sex	Number	Died	Average Age (Years)	Necropsies	Mortality (Percentage)	Recovered	Average Age (Years)
Male	303	199	32.5	184	65.5	104	29.5
Female	40	23	35.1	21	57.5	17	25.3
Total	343	222	33.8	205	64.7	121	27.4

TABLE 4.—*Data on Patients Who Had Laparotomies*

Sex	Number	Died	Average Age (Years)	Necropsies	Mortality (Percentage)	Recovered	Average Age (Years)
Male	268	169	31.9	155	62.6	99	25.9
Female	33	16	34.3	14	48.5	17	20.3
Total	301	185	33.3	169	61.4	116	27.6

TABLE 5.—*Data on Patients Who Had no Laparotomies*

Sex	Number	Died	Average Age (Years)	Necropsies*	Mortality (Percentage)	Recovered	Average Age (Years)
Male	35	30	32.6	29	85.7	5	27.7
Female	7	7	34.7	7	100.0	0	....
Total	42	37	33.7	36	88.0	5	27.7

* The one body not examined after death was that of the only patient among the 343 with no operation and no necropsy; 16 others had operations but no necropsies. The 17 were removed from the morgue by "orders from the Central Office."

with such wounds in fifteen years; 2 recovered. In 1 of these 2 the liver was the only viscus wounded. In the other, every coil of bowel had many small perforations, and about twenty shot were free in the abdomen. Willis[42] referred to 14 patients with shotgun wounds whom he saw at Rocky Mount, N. C.; 4 died and 3 recovered without operations; of the 7 who underwent laparotomies, 4 recovered. He also mentioned that when repairing the wounds made by a bullet in another patient he

41. Bunch, G. H.: Shotgun Wounds of the Abdomen, Tr. South. S. A. **41**:38, 1928.

42. Willis, B. C.: Penetrating Wounds of the Abdomen. Reporting Sixty-Three Cases Received from Pistol, Rifle and Shotgun Missiles, Ann. Surg. 96:1051, 1932.

found two bird shot in the liver and 1 in the gallbladder from a former shooting.

One of 4 patients with shotgun wounds reported on by Ewstifejewa [43] recovered. This patient had a generalized peritonitis when the laparotomy was performed three days after the shooting. Only a few perforations of the small bowel were found. The missiles in the cartridge were nails, and they had entered the lower part of the abdomen.

Most of the reports of shotgun wounds deal with single patients who recovered. Pels-Leusden's [44] patient had a thoraco-abdominal wound; the omentum, transverse colon and food-distended stomach entered the left pleural cavity through a huge rent in the diaphragm, and the spleen was in fragments. Another recovery reported by Waters [45] was that of a boy, aged 15, who was shot at close range. The stomach projected like a football carried under the left arm. In this patient also the spleen was extremely torn.

The patients of Foisy [46] and Cochez and Pieri [47] were both shot in the back; recovery was protracted, and two or more operations were performed.

A man who attempted suicide by shooting himself in the left hypochondriac region with a shotgun and was treated by Estes [48] left the hospital after fifty-six days, having undergone removal of the left kidney. Cannada,[49] on the other hand, in recording the data on bullet wounds in 7 patients included the wounds made by small shot in a Negress, who died seven days after he had repaired thirty-eight perforations in the small bowel, colon, stomach and gallbladder.

The purpose of this discussion of shotgun wounds is to emphasize the statement that they deserve a separate place, that they possess dis-

43. Ewstifejewa: Verletzungen der Bauchhöhle. Zusammenstellung des Materials des Smolensker Gouvernements-Krankenhauses für 2½ Jahre, 32 Fälle, Russk. vrach **12**:402, 1913.

44. Pels-Leusden: Milz und Zwerchfellverletzung, Verhandl. d. deutsch. Gesellsch. f. Chir. **33**:95, 1904.

45. Waters, C. H.: Gunshot Injury of the Thorax with Extrusion of the Entire Stomach and Laceration of the Spleen, J. A. M. A. **73**:1577 (Nov. 15) 1919.

46. Foisy, E.: Blessure de l'ampoule rectale et l'intestin grêle par coup de fusil de chasse. Laparotomie, suture de la porforation de l'intestin et exclusion du rectum. Occlusion intestinale le 38me jour par bride épiploïque. Section de la bride. Fermeture ultérieure de l'anus iliaque, Guérison. Bull. et mém. Soc. de chirurgiens de Paris, **39**:1410, 1913.

47. Cochez and Pieri (d'Alger); Plaie du duodenum par arme à feu; anus contra nature consécutif; gastro-entérostomie; guérison, Bull. et mém. Soc. d. chirurgiens de Paris **51**:503, 1925.

48: Estes: Case of Small Shot Wound of the Abdominal Cavity; Laceration of the Spleen, Mesocolon and Kidney, and Probably Laceration of the Stomach also; Recovery, Tr. Am. S. A. **17**:257, 1899.

49. Cannada, J. E.: Wounds of the Liver, Lancet-Clinic **57**:449, 1906.

tinctive features and that accounts of them should not be interwoven with those of bullet wounds.

The oldest patient in our series was a woman aged 70; the youngest, a boy aged 5 years; both recovered. Undoubtedly many factors contributed to the fact that the average age of the 343 patients wounded by bullets was 31.5 years. The relative youthfulness is of great interest and rather startling, but there is no justification for an attempt to discuss its causes here. Its influence on the mortality rate, 64.7 per cent, is indubitable.

Except for routine examination of the entire spinal cord, of the joints of the extremities and of the marrow of long bones, the postmortem examinations were quite thorough. All the important structures of the neck, including the large blood vessels, were examined. The parathyroid glands were not examined as a routine.

Microscopic examinations were made of the important viscera, of places with obvious gross disease, of the brain, of the brain stem and of the upper end of the spinal cord. At the time of the necropsy the removed brain was placed bottom uppermost in the skull cap and a dilute solution of formaldehyde U.S.P. (1:10) was run in the basilar and two middle cerebral arteries, first in one artery and then in another, clips being placed on the two vessels not receiving the solution at the time. The embalming was continued until the brain was firm. The brain was then placed in a jar containing solution of formaldehyde U.S.P. (1:10) for a week or two; then it was sectioned and examined grossly, and after that pieces were taken for microscopic study.

With few exceptions such necropsies were made on the bodies of 205 of the 222 patients who died. Of the 17 unexamined bodies, 1 was that of a patient who had not been operated on; the remaining 16 patients had undergone laparotomies. Some of these 16 were persons for whose suicide there was overwhelming evidence; the conditions in a few others were fully disclosed by the surgeons who also recovered the bullets. But most of the 17 bodies were unexamined by "orders from the Central Office." In other words, political or other influences prevented the necropsies. The total number of necropsies mentioned in the contributions briefly summarized in table 2 is only 146; undoubtedly many more were actually performed.

The 205 necropsies in our series (tables 4 and 5) include 169 bodies of the 301 patients who had laparotomies and 36 of the 37 who died without such operations. As far as could be ascertained clinically, most of the 42 patients who had no operations died of shock and hemorrhage. For the 36 whose bodies were examined after death the following data are recorded: 21 were moribund on entrance; the condition of 12 was poor; that of 2 was fair, and that of 1 was good. In this last patient, a man aged 45, the entrance wound was a little below the right nipple,

and the bullet lodged subcutaneously at a similar distance below the left nipple. Death occurred on the thirteenth day, and wounds were found in the ribs and liver; there were also a subphrenic abscess, pleuritis and pericarditis. Twenty-one of the 36 patients had one entrance wound, 11 had two such wounds, and 2 had three. Thirty-three of the 36 lived, on an average, for six hours after entrance into the hospital. Large blood vessels were found to be wounded in 17; in 7 of these the aorta was injured. The wounds in 12 patients were thoraco-abdominal, that is to say, both abdominal and thoracic organs were shot by the same bullet. In one patient a bullet passing through the scrotum made seven perforations in a loop of small bowel there in a hernial sac. The average number of organs injured in the 36 patients was three; in 1 patient a

TABLE 6.—*Mortality Resulting from Bullet Wounds of the Abdomen Involving (a) Only One Viscus and (b) Two or More Viscera* *

	Wounds of Single Viscera; Wounds of Large Blood Vessels				Wounds of Two or More Viscera			
Viscus	Number	Recoveries	Deaths	Mortality (Percentage)	Number	Recoveries	Deaths	Mortality (Percentage)
Stomach	15	13	2	13.3	63	13	50	79.3
Small intestine	41	21	20	48.7	100	22	78	78.0
Colon	17	9	8	47.0	83	14	69	83.1
Liver	28	24	4	14.3	52	7	45	86.5
Urinary bladder	3	1	2	66.6	15	1	14	93.3
Kidney	3	3	0	0.0	31	7	24	77.4
Blood vessels	1	0	1	100.0	23	2	21	91.3
Spleen	0	0	0	0.0	14	1	13	92.8
Pancreas	0	0	0	0.0	13	4	9	78.0

* Of the 301 patients with laparotomies, 37 of the 108 with wounds of a single viscus or of only large blood vessels died, a mortality rate of 34.2%. Of the 182 with wounds of 2 or more viscera (again including large blood vessels as viscera), 147 died—a mortality rate of 80.7%. Of 11 patients with unwounded viscera, 2 died; bullets entered the abdomen in these 11. There is overlapping in the right-hand part of the table. For example, the 63 patients with wounds of the stomach and other viscera are counted again with the patients in whom the other viscera were wounded.

huge hemoperitoneum was present, and a single abdominal organ was wounded. On the whole, subsequent developments and observations justified the decisions that laparotomies on the 42 patients in this group should not be made.

Only two other reports deal with large numbers of patients. One is by Camaggio,[50] who discussed the treatment given at the Pellegrini Hospital in Naples to 177 patients with bullet wounds of the abdomen; the other is an account by Billings and Walkling[51] of 114 cases in which laparotomies were performed at the Pennsylvania Hospital in Philadelphia (table 2).

50. Camaggio, F.: Altre 50 laparotomie per lesioni violente dell'abdome, Gior. internaz. d. sc. med. Napoli **37**:8, 1915.

51. Billings, A. E., and Walkling, A.: Penetrating Wounds of the Abdomen, Ann. Surg. **94**:1018, 1931.

Wounds of Single and Multiple and of Hollow and Solid Viscera; Wounds with One or More Bullets (*Tables 6, 7, 8 and 9*).—Patients with simple bullet penetration of the abdomen without visceral injury gener-

TABLE 7.—*Mortality Rate for Patients With a Single Wound and for Patients with More than One Wound of a Single Viscus*

	Single Wound				Multiple Wounds						
Viscus	Number	Recoveries	Deaths	Mortality (Percentage)	Number	Recoveries	Deaths	Mortality (Percentage)	Total Number	Total Mortality (Percentage)	Comment
Stomach	5	5	0	0.0	10	8	2	20.0	15	13.3	
Small intestine	4	1	3	85.0	37	20	17	45.9	41	48.7	
Colon	5	2	3	60.0	12	7	5	41.6	17	47.0	
Liver	24	21	3	12.5	4	3	1	25.0	28	17.2	
Urinary bladder	1	1	0	0.0	2	0	2	100.0	3	66.6	
Kidney	3	3	0	0.0	0	0	0	0.0	3	0.0	
Blood vessels	1	0	1	100.0	0	0	0	0.0	1	100.0	Mesenteric artery
Total	43	33	10	23.2	65	38	27	41.5	108	34.2	

TABLE 8.—*Mortality Rate After Laparotomies for (a) Wounds of Hollow Viscera, (b) Wounds of Solid Viscera, (c) Wounds of Both Hollow and Solid Viscera and (d) Simple Penetrating Wounds Without Visceral Injury*

Organs	Number	Recoveries	Deaths	Mortality (Percentage)
Hollow viscera	170	67	103	60.5
Solid viscera	36	27	9	25.0
Hollow and solid	84	13	71	84.5
Penetration of peritoneum only	11	9	2	18.1
Total	301	116	185	61.4

TABLE 9.—*Mortality Rates After Laparotomies for (a) Wounds with a Single Bullet and (b) Wounds with More than One Bullet* *

	Total	Recoveries	Deaths	Mortality (Percentage)
Patients with abdominal wounds from only one bullet	262	111	151	57.6
Patients with abdominal wounds from more than one bullet	14	2	12	85.7
Patients with abdominal wounds from one bullet and thoracic wounds from a second bullet	3	0	3	100.0
Patients with abdominal wounds from one bullet and wounds of the extremities from other bullets	22	3	19	86.9
Total	301	116	185	61.4

* One of 7 patients wounded in the upper part of the abdomen with more than 1 bullet recovered; 1 of 3 wounded in the lower part with more than 1 bullet recovered; 4 with bullets in both parts died. Only 1 of the 13 with wounds of the abdomen and upper extremities recovered; 2 of the 6 with wounds of the abdomen and lower extremities recovered; 3 with bullet wounds of the abdomen and both upper and lower extremities died. There were exit wounds in 32 of the 116 who recovered and in 62 of the 185 who died.

ally recover, except when infections develop in the path of the bullet; only 2 of the 11 patients (table 8) with such wounds died, both of peritonitis. Those with wounds of a single viscus (table 6) also usually

recover; this is especially true if the injured organ is solid. Of 108 patients with wounds of a single viscus (table 6), 37 died—a mortality rate of 34.2 per cent; of the 31 who had injuries of a solid organ 4 died—a mortality rate of 12.9 per cent; and for the 76 who had injuries of a hollow viscus the mortality rate was 42.1 per cent.

Wounds of the Stomach: In the 2 fatal cases of wounds limited to the stomach the interval between the injury and the operation was less than two hours; one patient died two hours after operation of hemorrhage; the other died twenty-two hours after operation of infection with gas bacilli. In cases of bullet wounds involving only the liver the mortality rate was also low; only 4 of 28 patients so shot died, all of complications. The only patients in this group with exit wounds were the 7 who recovered.

Wounds of the Intestine: There is a great deal of evidence that bullet wounds affecting solely the colon are much more serious than wounds elsewhere in the gastro-intestinal tract. This is not true in our series, but only 17 patients in our series had such wounds. The average number of perforations in the colon in the 8 patients who died was three; the highest number of such perforations in any one patient, nine. These wounds were made by a bullet which traversed the trunk from side to side. Vale [52] reported the occurrence of a similar path followed by a bullet in a patient in whom injury was confined to the mesentery. The average number of perforations in the colon in the patients in our series who recovered was two and five-tenths perforations per patient.

The largest group with wounds exclusively of a single abdominal organ consisted of 41 patients with injuries of the small bowel or of the small bowel and its mesentery. This is to be expected because of the relatively large space occupied by the small intestine. The mortality rate, 48.7 per cent, is quite high, and death was usually due to peritonitis. The average interval between the injury and the operation in the case of patients who died was four and six-tenths hours; for the remainder it was three hours. The number of perforations apparently fails to influence the outcome, for the average number of perforations per patient discharged was five and seven-tenths; for those who died the average number was five and three-tenths. The largest number of perforations in any single patient was fifteen, and six of these were found after death. Of patients who recovered, fourteen perforations was the highest number found in any one patient.

Wounds of Two or More Viscera: The true gravity of bullet wounds of the abdomen is displayed when two or more viscera are injured (table 6) and when the wounds are made by two or more bullets (table 9). Of the 301 patients in our series who had laparotomies, 182

52. Vale, C. F.: Civilian Wounds of the Abdomen, J. Michigan M. Soc. **22**:183, 1923.

had wounds of two or more viscera. Of these, only 35 recovered, and 147 died; this reveals an astounding mortality rate of 80.7 per cent, as compared to that of 34.2 per cent for those with injuries to a single viscus. Of 23 who had wounds of viscera and large blood vessels, 21 died—a mortality rate of 91.3 per cent. The mortality rate was likewise high when the kidneys, pancreas and spleen were wounded together with other organs.

Wounds of the Kidneys: Of the 343 patients in our series, 43 had bullet wounds of the right or left kidney; in no patient were there wounds of both kidneys. In 29 patients the left and in 14 the right kidney was injured. Operations were performed on 34 of the 43 patients; 10 of the 34 recovered and 24 died—a mortality rate of 70.6 per cent. Billings and Walkling [51] in their series of 114 patients with bullet wounds of the abdomen treated by laparotomy had 10 with wounds of the kidney; 3 recovered and 7 died—a mortality rate of 70 per cent. Of the 24 patients in our series who died after laparotomy, 19 were shot in front and 5 were shot from behind; 15 died of hemorrhage and shock, 8 of peritonitis and 1 of separation of the laparotomy wound. Of the 10 who recovered, 6 were shot in front and 4 from behind. In 3 patients in whom the kidney alone was injured, the bullet traversed the abdomen. These 3 recovered. In 31 patients other viscera also were injured; the stomach was injured in 16 patients, the colon in 12, the liver in 10, the small bowel in 9, the pancreas in 3, the spleen in 2, and each lung and each adrenal gland in 1 patient, respectively.

Wounds of the kidney overlooked by the surgeon at the time of operation were found subsequently at autopsy in 18 of the 24 patients who underwent operations. In 4 of 7 patients who died and had undergone operations, Billings and Walkling [51] found such overlooked wounds. In the 18 patients of our series, wounds of the left kidney were overlooked in 11 and wounds of the right kidney, in 7. Hemorrhage and shock accounted for death in 13 patients; generalized peritonitis caused death in 4, and separations of the laparotomy wound caused it in 1. The 9 patients who were not operated on died, and all had wounds of other viscera besides wounds of the kidneys; 4 were shot from behind and lived for an average period of two and a half days; 5 who were shot in front lived for an average period of three hours.

Wounds of the Pancreas: There are relatively few reports of cases dealing with peace time bullet wounds of the pancreas whether alone or associated with wounds of other viscera. At the time he made his report Becker [53] stated that his was the only case in the literature in which the pancreas was the sole viscus injured. Berendes [54] attended a patient

53. Becker, A.: Isolierte Schussverletzung des Pancreas, durch Operation geheilt, Beitr. z. klin. Chir. **44**:748, 1904.

54. Berendes: Pankreasschuss, Centralbl. f. Chir. **38**:163, 1911.

with a bullet wound limited to the pancreas and located at the junction of the middle and distal thirds. In discussing this report, Nordman related his experiences in operating on a woman for an isolated wound of the pancreas two weeks after she had attempted suicide. Guleke [55] found reported in the literature only 31 cases of wounds of the pancreas; in 24 of these operation was performed; 11 patients recovered and 13 died.

In order to find any comprehensive investigation of bullet wounds confined to the pancreas one has to turn to the experiences related by military surgeons of the World War. The study of Wallace [56] on 965 patients who underwent laparotomy for wounds of the abdomen caused by missiles used in war disclosed that wounds of the pancreas alone were present in only 5 and that in 3 other viscera besides the pancreas were wounded. Fraser and Drummond [57] in studying material from a similar source found one patient with an injury to the pancreas among 300 with wounds of the abdomen made by missiles used in war.

In our series there were 19 patients with bullet wounds of the pancreas, and in all these wounds occurred in combination with injury of other organs; 15 died and 4 recovered—a mortality rate of 78 per cent. Of the 19 patients, 13 had laparotomies; 4 recovered and 9 died—a mortality rate of 69.2 per cent. The associated visceral injuries in these 13 patients were as follows: nine wounds of the stomach; six wounds of the liver, five wounds of the small bowel, three wounds of the diaphragm and one wound of the inferior vena cava. On admission, 5 patients were in good condition: 2 of these died, 1 lived for one and a half days and died of hemorrhage and another died of peritonitis after seven days. Of 4 patients admitted in fair condition, 3 died, 1 dying on the operating table, another of hemorrhage seventeen hours after operation, and a third of peritonitis six days after the operation. Of 4 patients who were moribund on admission, 3 died of shock and hemorrhage and 1 died of peritonitis three days after the operation. In 9 bodies sixteen wounds overlooked by the surgeon were found at autopsy: seven wounds were in the pancreas, three were in the liver, two were in the left kidney and there was one in the right kidney, stomach, small bowel, and common bile duct, respectively. Fat necrosis was noted in 4 of these bodies. In the patients who recovered the stomach was wounded three times, the small bowel two times and the liver and diaphragm each once.

The 6 patients with wounds of the pancreas who did not undergo laparotomy died. All were moribund on admission to the hospital and

55. Guleke: Pankreasschuss, Med. Klin. **10**:131, 1914.

56. Wallace, C.: A Study of 1,200 Cases of Gunshot Wounds of the Abdomen, Brit. J. Surg. **4**:679, 1917.

57. Fraser, J., and Drummond, H.: Three Hundred Perforating Wounds of the Abdomen, Brit. M. J. **1**:321, 1917.

died within five hours or less. In the bodies of these 6 patients twenty-five wounds were found at autopsy; among others six wounds were in the liver, three each in the stomach, left kidney and aorta, and one each in the left lung, renal vein, splenic vein and inferior vena cava.

Wounds of the Spleen: As for bullet wounds of the spleen, we wish solely to direct attention to their infrequent occurrence and to the high mortality rate incident on such wounds. As regards the former, the small size of the spleen and its protected position are important factors. The high mortality rate is due to the vascularity of the organ and to the fact that other closely adjacent important viscera are wounded also. The collection by Schaefer [58] in 1902 included both peace time and war time wounds in 71 patients, 20 of whom had laparotomies; 13 died and 7 recovered—a mortality rate of 65 per cent. Only 1 patient had a wound solely of the spleen. With considerable duplication Girgolaw [59] collected reports on 69 patients with bullet wounds of the spleen; he found only 2 with wounds solely of the spleen; 39 died—a mortality rate of 56.5 per cent. In his long article, Guibe [60] analyzed 108 reports from the literature on bullet wounds of the spleen. Many of the cases are from military surgical practice. In practically all the patients other organs were wounded in addition to the spleen. Among the 112 patients with bullet wounds of the abdomen, Loria [28a] found either at operation or at necropsy only 3 who had wounds of the spleen. One in whom only the spleen was injured recovered; 2 with additional wounds of other viscera died. No wounds of the spleen were found in the 58 patients with bullet wounds of the abdomen who underwent laparotomy studied by Willis.[42]

In our series, only 19 patients had bullet wounds of the spleen; in these the wounds occurred in combination with wounds of other viscera; 14 had laparotomies, and 5 had no operations. Of the 14 operated on, 1 recovered—a mortality rate of 92.8 per cent. The 5 who were not operated on died. Of those who underwent laparotomy, 11 were moribund on entrance to the hospital; only 3 were in fair condition. The interval between the injury and the operation was four hours or less for 10 patients, and for 4 others it was eight hours, seventeen hours, twenty-three hours, and forty-eight hours, respectively.

In the first twenty-four hours after operation, 10 of the 13 patients who died succumbed to hemorrhage and shock; 2 died on the table; 1 died two days after operation and was not examined post mortem; 2 died

58. Schaefer, F.: Die offenen Milzwunden und die transpleurale Laparotomie, Beitr. z. klin. Chir. **36**:761, 1902.

59. Girgolaw, S. S.: Zur Frage zu den Schusswunden der Milz, Vrach. gaz. nos. 46 and 47, 1909; abstr., Zentralbl. f. Chir. **7**:255, 1910.

60. Guibe, M.: Les plaies de la rate par coup de feu, Clinique, Paris **7**:435, 1912; Rev. de gynéc. et de chir. abd. **18**:491 and 583, 1912.

of peritonitis three days and seven days after operation, respectively. The bodies of 12 of the 13 patients who died were examined post mortem. In 1 patient, one other viscus besides the spleen was injured; in 3, two others; in 7, three others, and in 1, four others, respectively, were injured, making a total of thirty-two wounds of the viscera in addition to the wounds of the spleen in the 12 patients. There were eleven wounds of the diaphragm and thirty-two additional wounds of the viscera, as follows: of the stomach, ten; of the liver, seven; of the colon, five; of the small bowel, four; of the left lung, four; of the right lung, one, and of the left adrenal gland, one. In 11 of the 12 bodies examined post mortem wounds overlooked or not mentioned by the surgeon were found as follows: three in the spleen; five in the stomach, four in the liver, four in the left lung and one each in the small bowel, left kidney and left adrenal gland, making a total of nineteen overlooked wounds.

The 5 patients not operated on who had wounds of the spleen also had wounds of the thorax and are included in the group of patients with thoraco-abdominal wounds (table 10).

Wounds Caused by a Single Bullet: The small number of patients shot with more than one bullet is surprising, for a rapid succession of shots with modern firearms, such as the automatic pistol, may be executed with nearly the same ease as the firing of a single shot. Willis [42] reported the occurrence of wounds from a single bullet in all but 8 of his 58 patients. In our series, 262 of the 301 patients (table 9) who underwent operations had abdominal wounds made by one bullet only; of these, 151 died—a mortality rate of 57.6 per cent. This added trauma to the abdomen by a second or third bullet is pronounced and highly fatal, as shown by the fact that the mortality rate for that group was 85.7 per cent. There is a higher mortality rate, 96.9 per cent, for 22 patients who had abdominal wounds from one bullet and wounds of the extremities by other shots. The 3 patients with wounds of the abdomen made by one bullet and with injury of the thorax by a second died. It is quite obvious that prompt operation and a minimum period of anesthesia are of little avail in cases in which such a multiplicity of wounds is present.

Thoraco-Abdominal and Abdominothoracic Wounds (Table 10).—Bullets entering the thorax and passing through the diaphragm into the abdomen or in a reverse direction, from the abdomen into the thorax, produce wounds usually referred to as thoraco-abdominal, although the latter are frequently termed abdominothoracic. Both terms deserve a place because the injuries are likely to be more severe in the first segment of the trunk wounded, the force of the bullet being somewhat expended in the second. Both terms refer to wounds made by a single missile, although the wounds of the thorax and abdomen and their viscera made by a single shot from a shotgun carrying either bird shot or

buck shot would be properly designated thoraco-abdominal or abdominothoracic when both parts of the trunk are wounded. The wounds confined to the thorax and made by one bullet and those made by a second shot fired into the abdomen are neither thoraco-abdominal nor abdominothoracic; they are bullet wounds of the thorax and abdomen. One essential of thoraco-abdominal or abdominothoracic wounds is that the diaphragm is wounded. This wound is sometimes so close to its attachment that the path of the bullet is mainly in the inner part of the wall of the trunk.

Of the 31 patients who were operated on (table 10) 19 had thoraco-abdominal and 12 abdominothoracic wounds. In the 12 patients who were not operated on the wounds were thoraco-abdominal. Of the 31 patients who were operated on 25 were males. The youngest patient in that group was a girl aged 17; the oldest, a man aged 68. The average age of the 31 patients was 33 years. Only 1 of 20 patients whose condition was poor on entrance recovered; of 6 who entered in a fair condition, 2 recovered, as did 4 of the 5 whose condition on entrance was good. Two of those who underwent laparotomies died on the table; 9 died during the first twelve hours; two died during the second twelve hours, and 4 died on the second day. Why one patient lived five and another thirteen days without undergoing laparotomy was not learned. The patient who lived four days had an operation for the removal of a bullet from the left femoral artery. This is referred to in another part of the article.

In view of the high mortality it is pertinent to recall that Moorhead [61] while still an intern at the Cook County Hospital repaired the wounds in a 45 year old man who in attempting suicide so shot himself that the bullet, passing in above the left sixth rib in the nipple line, went through the diaphragm at the upper part of the spleen, again through the diaphragm and through the lower edge of the left lung. It then broke the left tenth rib and lodged against it. The man recovered. The operation was performed on Nov. 28, 1891, soon after admission. The shooting took place seventeen hours before entrance. The surgeon, J. B. Murphy,[62] in his oration on "Surgery of the Lung" at the meeting of the American Medical Association in Denver in 1898 referred to the opportunity the operation afforded of observing the way respiration affected the lung when the thorax was opened.

A large part of the information about thoraco-abdominal wounds has come from experience gained during the World War.[63] At that time it

61. Moorhead, E. L.: Gunshot Wound of the Thorax and Spleen, Chicago M. Rec. **2**:549, 1892.

62. Murphy, J. B.: Surgery of the Lungs, J. A. M. A. **31**:151 (July 23) 1898.

63. Bowlby; Voncken, J., Duval, P., and Jacob, Depage: Plaies thoraco-abdominales, Arch. de méd. et pharm. mil. **69**:341, 1918.

was learned that the wounds are usually on one side, that the size of the hole in the diaphragm is of great importance, that hernia of abdominal viscera into the thorax occurs chiefly on the left side and that blood

TABLE 10.—*Thoraco-Abdominal and Abdominothoracic Wounds in 43 Patients*

Patients with Laparotomies (31)			Patients Without Operations (12)		
Organs Injured	Number of Patients	Comment	Organs Injured	Number of Deaths	Comment
Diaphragm..	31	24 died; 7 recovered; 20 were moribund on entrance; all were shot with one bullet; the average injury-operation interval for those who recovered was 3.7 hrs.; for those who died it was 4.8 hrs; in 19 of the 23 bodies examined after death wounds overlooked by the surgeons were found	Diaphragm..	12	All 12 died; necropsies were performed on all; 9 of the 12 were moribund on entrance; all were shot with one bullet; 8 died at an average of 7.5 hrs. after entrance; one lived 1 day, one 4 days, one 5 days, and one 13 days
Liver.....	16		Liver.....	7	
Stomach.....	16		Stomach.....	4	
Spleen.....	10		Spleen.....	5	
Left lung....	6		Left lung....	3	
Large blood vessels.....	5		Large blood vessels.....	2	
Small bowel.	4		Small bowel.	1	
Colon.....	4		Colon.....	1	
Left adrenal gland.....	4		Left adrenal gland.....	0	
Right kidney	3		Right kidney	0	
Right lung...	2		Right lung...	3	
Pancreas....	2		Pancreas....	0	
Spinal cord..	1		Spinal cord..	1	
Esophagus..	0		Esophagus..	1	
Left kidney..	0		Left kidney..	3	

TABLE 11.—*The Influence on the Mortality Rate of the Place of Entrance of Bullets and the Direction of Their Paths in Patients Who Had Laparotomies* *

	Upper Part of the Abdomen			Lower Part of the Abdomen			Upper and Lower Parts of the Abdomen			Summary			
Direction	Recoveries	Deaths	Mortality (Percentage)	Recoveries	Deaths	Mortality (Percentage)	Recoveries	Deaths	Mortality (Percentage)	Recoveries	Deaths	Mortality (Percentage)	Total
Front to back.....	64	92	59.0	24†	42	63.6	0	7	100	88	141	61.5	229
Back to front.....	12	15	55.5	12‡	16	57.1	..	..	...	24	31	56.3	55
Side to side.....	3	3	50.0	1	7§	87.5	..	..	...	4	10	71.4	14
Front and side....	..	3	100.0	..	..	....	..	..	...	..	3	100.0	3
Total.....	79	113	58.8	37	65	63.6	0	7	100	116	185	61.4	301

* Among the 92 patients who died from front to back wounds of the upper part of the abdomen 5 were shot in the abdomen with 2 bullets; both bullets had a front to back course.

† One patient of the 24 who recovered from bullet wounds of the lower part of the abdomen was shot in that region with 2 bullets passing in from the front.

‡ An exceptional recovery occurred in a patient in this group who was shot from behind with 3 bullets.

§ Each of the 7 patients who died from wounds of both the upper and the lower parts of the abdomen was shot with two bullets.

usually escapes from intrathoracic wounds into the abdomen so that the lungs are not immobilized by hemothorax.

Paths of Bullets (*Table 11*).—Of the 301 patients who underwent laparotomies, 229 were shot in front; in 156 of these the wound was in the upper part of the abdomen; in 66 it was in the lower part, and 7 had a bullet in each location—the mortality rates were 59 per cent, 63.6 per cent and 100 per cent, respectively. Whether the internal

wounds were of the upper or lower part of the abdomen, the mortality rate, 57.1 per cent, was less for patients shot from behind. The number of persons shot from one side is so small that the mortality rate has no significance. Apparently, many persons die when bullets pass across the lower part of the trunk, and more die from injuries caused by bullets passing from front to back and wounding the lower part of the abdomen than from similar injuries of the upper part of the abdomen. In the latter case the bullet passes through more solid viscera. Of course, in cases in which there is an exit wound or recognized subcutaneous lodgment at the end of a path through the trunk, surgeons of experience make quite accurate surmises as to the organs injured. Martin and Hare [10] contended that bullets are deflected by soft tissues. It is also possible that some paths are irregular because the bullets tumble end over end or because their force is about spent. In the cases forming the basis of this report the weapons were usually revolvers or pistols, not rifles, and consequently less than one third of the patients in our series had exit wounds. Only 8 of the 50 patients in Goltman's series [64] had exit wounds.

Lodgment of the bullet just beneath the skin after it has traversed the trunk implies that the driving force was exhausted. The toughness of the corium may also be recalled; from it leather is made. Some other information pertinent to, but not included in, the table concerns exit wounds and their absence. In 178 patients there were no wounds of exit; the mortality rate for that group was 59.1 per cent. In 29 patients the bullets lodged subcutaneously; the body was practically traversed. If these cases are added to the 94 in which exit wounds were present, the sum is 123, or 40.8 per cent of the 301 cases in which laparotomies were performed; for this group the mortality was 64.2 per cent. It seems reasonable to conclude that the greater force required to send bullets on through the body, or even to subcutaneous lodgment opposite the wound of entrance, causes more damage than less forceful shots. Another noteworthy phase of these matters, of course, is the fact that bullets have been known to drop out of the clothing when the patient or dead body is undressed. Although the mortality rate from injuries caused by bullets which traverse the trunk is higher by about 5 per cent than that from the other wounds, even this small difference has definite value because of the large number of patients concerned. The paths of a few bullets were unusual.

One crossed the body from right to left, the entrance and exit wounds being symmetrical in the nipple lines just above the costal margins, and passed through both lobes of the liver. A second patient had a wound

64. Goltman, M.: One Year's Experience (1916) with Gunshot Wounds of the Abdomen at the Memphis General Hospital, Surg., Gynec. & Obst. **26**:217, 1918.

of entrance in the right posterior axillary line just above the ninth rib, wounds of the diaphragm and liver, and lodgment of the bullet in the scrotum. Both patients recovered.

Overlooked Wounds (Table 12).—The term "overlooked wounds" has only relative precision, for it undoubtedly is applied here to some wounds which were noted by the surgeons but unmentioned in the hospital record. The surgeons were not always present when the postmortem examinations were made. Many of the shootings were criminal, and the necropsies necessarily had a limited audience. A pair of unrepaired bullet perforations of a loop of the small bowel found after death has a significance different from that of an overlooked grooving

TABLE 12.—*Overlooked Wounds of the Diaphragm and Abdominal Viscera Found at the Postmortem Examination of Patients who Underwent Laparotomies*

	Diaphragm	Colon	Small Bowel	Urinary Bladder	Major Blood Vessels	Left Kidney	Right Kidney	Liver	Left Lung	Stomach	Pancreas	Common Bile Duct	Rectum	Spleen	Left Adrenal Gland	Right Adrenal Gland	Left Ureter
Number of bodies with overlooked wounds of one viscus.....	2	13*	10	6	6	5	4	3	3	1	1	0	1	1	1	0	0
Number of bodies with overlooked wounds of more than one viscus†...	13	10	6	3	11	7	5	11	8	7	6	1	2	3	3	2	1
Total number of overlooked wounds of each viscus.....	15	35	22	11	18	12	9	14	11	9	7	1	4	4	4	2	1

* In one body of this group of 13 there were also 2 laparotomy sponges.

† The figures in this row are overlapping. For example, if there were 10 bodies with overlooked wounds of the colon and in the same bodies overlooked wounds of other viscera, these 10 bodies are counted in other places in this row. A body with overlooked wounds in the colon and small bowel has a place in the vertical volumns for each viscus; it is counted twice. There were overlooked wounds of the colon in 23 bodies, but in some bodies the wounds numbered 2 or more, totaling altogether 35 wounds in 23 bodies. The overlooked wounds numbered 164 in 94 bodies; in 55 bodies there were overlooked wounds of a single viscus, and in 39 bodies there were overlooked wounds of two or more viscera.

perforating wound made by a bullet in the back wall of the colon close to the spleen. This difference acquires greater significance when the pair of in and out unrepaired perforations made by a bullet in a loop of the small bowel are associated with many other repaired perforations in other loops.

One may not be surprised to find overlooked wounds when patients die on the operating table. In the bodies of 11 of the 13 patients who died under such circumstances there were wounds unmentioned in the hospital records. When some of the necropsies were made not all of the observations by the clinicians had been entered on the records accompanying the body to the morgue. In addition to the 13 patients who died on the operating table, 87 others died during the first twenty-four hours after laparotomy, making a total of 100 of the 169 (table 4) who

underwent laparotomies and whose bodies were subjected to postmortem examination. The belief that many of these patients were severely injured when the operations were performed and were suffering from hemorrhage from shock or from both is supported by these figures. In the 169 bodies (table 12) there were overlooked wounds in 94; in the remaining 75 no overlooked wounds were found.

One factor which played a small but definite part in accounting for the number of bodies with overlooked wounds was the experience of the surgeons. At the Cook County Hospital there have been two resident surgeons for many years. Naturally, they were at hand for these emergency operations. Together they performed laparotomies on 184 patients with bullet wounds of the abdomen. The mortality rate for that group was 57.6 per cent. The mortality rate for 107 patients on whom laparotomies were done by thirty-five other surgeons was 69.1 per cent. In 10 cases the name of the surgeon who performed the operation was not recorded. One of the thirty-five surgeons performed laparatomies on 12 patients, another on 7, three on 6, five on 5, and so on down to the twelve who each performed a single laparotomy.

The influence of experience is also more directly shown by the presence of overlooked wounds in 54.4 per cent of the patients whose operations were performed by the two resident surgeons, whereas the thirty-five other surgeons overlooked wounds in 57.1 per cent of the patients. The difference is small, but the large numbers concerned in the calculations compel some respect for the conclusions. We do not pretend to know all the reasons for the presence in so many bodies of overlooked wounds. Perhaps careful attention to such details in a similar study of the work of any other large urban hospital would disclose corresponding conditions. There were undoubtedly some overlooked wounds in some of the patients who recovered. The exit wound in the back wall of the stomach is not always repaired, and after a time the bullet is removed from the soft tissues of the back.

The Interval Between the Injury and the Operation (Table 14).—The importance of a short interval between the injury and the operation gained recognition simultaneously with the importance of laparatomy. Surgeons soon learned that hemorrhage from a fair-sized blood vessel and peritonitis from a leaking intestine accounted for most of the deaths and that both should be repaired as soon as possible. In the earliest tables compiled by Morton,[13] Coley,[65] MacCormac [19] and others [66] attention was called to the value of a short interval between the injury and the operation in lowering the mortality rate; and this was recently reempha-

65. Coley, W. B.: Treatment of Penetrating Shot-Wounds of the Abdomen, Boston M. & S. J. **119**:373, 1888.

66. See table 1.

sized by Lewis.[67] Of the 30 cases recorded in the table by MacCormac, for example, the average interval between the injury and the operation for patients recovering was eight hours and for those dying, twenty-one hours. The same relationship obtains in many subsequent reports except that the interval for both those recovering and those dying has been shortened. For the 17 of the 23 patients in Marks'[68] series who recovered the average interval was three and seven-tenths hours, and for those dying, five and six-tenths hours. Prey and Foster[69] reported even shorter periods for their 22 patients; one and eighty-eight hundredths hours for those recovering, and three and four-tenths hours for those dying.

For most of the patients in our series the interval was short. Over 77 per cent of the patients were operated on within three hours after injury and the mortality rate for that group was 60 per cent; for those who were operated on after three hours the mortality rate was 65 per cent. The proximity to and availability of competent hospital and

TABLE 13.—*Mortality Rate; Condition on Admission and Laparotomies*

Condition	Number	Recovered	Died	Mortality (Percentage)
Good	66	46	20	30.3
Fair	123	55	68	55.3
Poor	112	15	97	86.6
Total	301	116	185	61.4

surgical care in large cities usually provide a short interval between the injury and the operation. Naturally, some long intervals are due to prolonged clinical observations.

Anesthesia.—Apparently the influence of anesthesia is not evident unless it is prolonged (table 15). The high mortality rate for the 27 patients anesthetized for thirty minutes or less was due to their critical condition. Some died on the operating table soon after the operation was begun. With few exceptions the anesthetic used was ether. The average time of anesthesia for the patients who recovered was seventy-one and six-tenths minutes; for those who died it was seventy-six minutes. One patient who died had only a local anesthetic.

67. Lewis, Dean, in discussion on Lewis, Dean, and Trimble, I. Ridgeway: Subcutaneous Injuries of the Abdomen, Ann. Surg. **98**:685, 1933.

68. Marks, H.: Penetrating Gun-Shot Wounds of the Abdomen, Tr. M. A. Missouri, 1893, p. 324; Gunshot Wounds of the Stomach; Laparotomy; Death, St. Louis Courier Med. **11**:11, 1894; Operations on Gunshot Wounds of the Abdomen, ibid. **12**:14 and 41, 1895.

69. Prey, D., and Foster, J. M.: Gunshot Wounds of the Abdomen, Ann. Surg. **99**:265, 1934.

Postoperative Drainage (*Table 16*).—The question whether laparotomy wounds should be drained and the factors which decide this question have been and still are a subject of controversy among surgeons. The contentions have concerned many conditions other than those due to bullets and have naturally centered about the presence or absence of a grossly evident inflammatory exudate on the peritoneum. This subject of drainage is another detail regarding which the information we possess

TABLE 14.—*The Interval between the Injury and the Operation*

Interval (Hours)	Total	Recovered	Died	Mortality (Percentage)
0-2	164	72	92	56.1
2-4	92	29	63	68.4
4-6	8	4	4	50.0
6-9	7	2	5	71.4
9-20	14	4	10	71.0
No data	16	5	11	68.0
Total	301	116	185	61.4

TABLE 15.—*Mortality Rate and Duration of Anesthesia*

Length of Anesthesia (Minutes)	Number	Recovered	Died	Mortality (Percentage)
0-30	27	10	17	62.9
30-60	106	43	63	59.4
60-90	95	37	58	61.0
90-120	56	22	34	60.7
120-150	17	4	13	77.0
Total	301	116	185	61.4

TABLE 16.—*Relation to the Mortality of (a) Drainage of the Laparotomy Wound and (b) No Drainage*

Management	Total Patients	Recovered	Died	Mortality (Percentage)
With drainage	108	42	66	61.1
Without drainage	87	38	49	56.3
No information	106	36	70	66.0
Total	301	116	185	61.5

is of importance because the number of patients dealt with is larger than usual (table 16). The abdomen was closed with drainage more frequently when the bullet wounded more than a single viscus. Of 108 patients with wounds of only one viscus, drainage was resorted to for only 30. Twenty of the 30 had wounds of either the stomach or bowel; of 182 patients with wounds of two or more viscera the wounds were drained in only 58. Records of the presence or absence of peritonitis or of peritoneal contamination by foreign bodies, feces, etc., at the time of operation unfortunately are too few to be used in attempts to estimate

the part played by drainage or its absence on mortality. Apparently drainage did not have a large influence on the mortality.

Causes of Death (Tables 17 and 18).—The severity of the injuries and the operations required both contributed to the mortality rate of

TABLE 17.—*Data on 205 Necropsies*

Patients with Laparotomies (169)	Number with Overlooked Wounds	Number with No Overlooked Wounds	Totals	Patients with No Laparotomies (36)	Totals
Acute generalized peritonitis	45	46	91	4	95
Shock and hemorrhage	44	26	70	31	101
Bronchopneumonia	2	0	2	0	2
Spontaneous evisceration	1	0	1	0	1
Systemic infection with gas bacilli	0	1	1	1	2
Ascending inflammation of the urinary organs	1	0	1	0	1
Phlegmonous inflammation about the urinary bladder	1	0	1	0	1
Pneumothorax on right side	0	1	1	0	1
Subphrenic abscess	0	1	1	0	1
Totals	94	75	169	36	205

TABLE 18.—*Bullet Wounds of Blood Vessels and Concomitant Visceral Injuries*

	Data on the 24 Patients with Laparotomy and Injuries to the Blood Vessels with Associated Visceral Injuries													Data on the 17 Patients with No Operations, with Injuries to the Blood Vessels and Associated Visceral Injuries											
Injured Blood Vessels	Small Bowel	Liver	Stomach	Pancreas	Urinary Bladder	Left Kidney	Colon	Common Bile Duct	Left Adrenal Gland	Left Lung	Spinal Cord	Total		Small Bowel	Liver	Stomach	Pancreas	Urinary Bladder	Left Kidney	Right Kidney	Colon	Spleen	Esophagus	Left Lung	Right Lung	Total	Grand Total
Inferior vena cava	4	1	4	3	0	0	2	1	0	0	0	8		1	1	1	0	0	0	0	0	0	0	0	0	2	10
Iliac blood vessels	4	0	1	0	1	0	0	0	0	1	1	5		3	0	1	0	3	0	0	0	0	0	0	0	5	10
Aorta	1	2	1	0	0	0	0	0	0	0	0	2		1	5	2	2	0	2	0	1	1	1	1	0	7*	9*
Mesenteric blood vessels	3	4	1	0	0	1	1	0	1	0	0	7		0	0	0	0	0	0	0	0	0	0	0	0	0	7
Renal blood vessels	0	0	1	0	0	0	0	0	0	0	0	1		0	1	1	1	0	1	0	0	0	0	0	0	1*	2*
Left femoral vein	0	0	0	0	0	0	0	0	0	0	0	0		1	0	0	0	0	0	0	0	0	0	0	1	1	1
Right subclavian artery	0	0	0	0	0	0	0	0	0	0	0	0		0	1	1	0	0	0	0	0	0	0	0	1	1	1
Left internal pudic artery	1	0	0	0	1	0	0	0	0	0	0	1		0	0	0	0	0	0	0	0	0	0	0	0	0	1
Splenic vein	0	0	0	0	0	0	0	0	0	0	0	0		0	1	1	1	0	1	0	0	0	0	0	0	1*	1*
Heart	0	0	0	0	0	0	0	0	0	0	0	0		0	1	0	0	0	0	1	0	0	0	1	1	1	1
Total	13	7	8	3	2	1	3	1	1	1	1	24		6	10	7	4	3	4	1	1	1	1	2	2	17	41

* One patient had wounds of the aorta, the splenic and left renal veins and had no laparotomy. In the remaining 40 one large blood vessel was wounded.

69.1 per cent for resections in 23 patients: in 1 patient resection of the spleen, in 2 patients, of the gallbladder, in 3 patients, of portions of the jejunum, in 4 patients, of one kidney, and in 13 patients, of segments of the ileum, was performed. Seven of the 23 patients recovered. In 17 of the 23 there were wounds in places other than the parts removed.

Of these 17 patients, 16 are included in the 169 who died after laparotomies and whose bodies were examined after death. Eight of the 169 died of miscellaneous causes: bronchopneumonia, spontaneous opening of the laparotomy wound and evisceration, ascending infection of the urinary organs, etc., as set forth in table 17. The patient with the subphrenic abscess was a woman shot with three bullets, one in each upper and one in the lower right abdominal quadrant; death occurred forty-four days after the patient was wounded. The phlegmonous inflammation about the urinary bladder spread, and a generalized peritonitis resulted; there was an unrepaired exit wound, and death occurred fourteen days after entrance.

The pneumothorax followed wounds made by a bullet which entered the left lumbar region, passed through the twelfth thoracic vertebra, left lobe of the liver and diaphragm and lodged in the right seventh intercostal tissues, 2.5 cm. from the sternum; large hemorrhage in the diaphragm and right perirenal tissues occurred; 430 Gm. of blood was present in the right pleural cavity, and there was a huge pneumothorax compressing the right lung.

There was no acute peritonitis associated with the systemic infection due to gas bacilli. Two laparotomy sponges were found in 1 body. After most of the bloody fluid was squeezed out of them, one weighed 28 and the other 83 Gm. That patient's death occurred six hours after operation; the left humerus had been broken by a second bullet; a segment of the ileum was resected, and an unrepaired bullet hole of the sigmoid flexure was found after death.

This death is recorded under the heading of shock and hemorrhage in table 17. Under the heading of acute generalized peritonitis in that table are listed deaths of 2 other patients in whose bodies laparotomy sponges were found after death. One patient died twenty-two hours, the other, one and a half days, after laparotomy. The sponges in these bodies were of the same size, and after most of the fluid they contained had been expressed each sponge weighed 120 Gm. The man who lived one and a half days had two segments of ileum resected, one 12.5 and the other 20 cm. long. The peritonitis was associated with infection due to gas bacilli. In the other body hemoperitoneum from a bullet wound of the left external iliac vein was present; the wound was repaired. Except in the last of the 3 patients, the sponges left in the abdomen probably played no part in bringing about death.

Another death from peritonitis occurred seven days after an operation. A loop of the small bowel 147 cm. distal to the duodenojejunal junction was caught and sutured to the abdominal wall in closing the laparotomy wound. The suture caught the loop opposite the mesenteric attachment. In comments on table 12 some allusion is made to the

part overlooked wounds have in causing peritonitis. We believe that such wounds occurring in the colon deserve a high place in any consideration of the dangers resulting from overlooked wounds.

We found in some records that the surgeons had mentioned the presence of feces in the abdomen or of foreign material such as cartridge wadding or fragments of cloth. But such observations were seldom mentioned, and the absence of such soiling of the peritoneum was not included in the protocols; from such sources the cause of the peritonitis remains unexplained. The figure for deaths resulting from peritonitis (91) and those for death resulting from hemorrhage and shock (70) are only approximate (table 17). The surgeons and the pathologist noted that some bleeding had taken place from wounds of patients in whom peritonitis subsequently developed. An added difficulty is the presence of overlooked wounds in about one half of these 161 bodies. It is impossible to assign each death to any single definite cause.

The most conclusive results were obtained in cases in which death was known to be due to hemorrhage. It will be recalled that of the 343 patients in our series, 42 had no operations, and that of these, 37 died and only 1 was not examined at necropsy. Naturally, deaths from bleeding would be regarded as the reason for failure to explore the abdomen of these 42 patients and attempt repair of the wounds. In the postmortem examinations of 36 of these 42 bodies, evidence of severe hemorrhage was found in 17 [70] (table 18). Just how many of these patients would have recovered after laparotomy and ligation of the bleeding vessels is speculation, but Lewis [67] stated that when it is a question of shock or hemorrhage he would first control the hemorrhage and then give a transfusion. The aorta was wounded in 7, the left common iliac artery in 3, the inferior vena cava in 2 and the left internal iliac vein, the left external iliac vein, the left femoral artery, the right subclavian artery, the left renal vein, the splenic vein, and the heart each in 1 body.

Sixteen of the 17 patients arrived moribund; 10 were shot with one bullet, 6 with two, and 1 with three. In the patient shot with three, all three bullets entered in front, causing wounds of the aorta, left renal vein and splenic vein as well as of the stomach, liver, pancreas and left kidney. In the others (16) only one large blood vessel was wounded in 15; in 1 the heart was injured. Sixteen of the 17 patients lived for an average of two and three-tenths hours after entrance; the seventeenth lived for four days. This was a middle-aged man shot by his son: there were entrance and exit wounds in the upper part of the left arm, with bullet paths connecting the wounds for two bullets. When the arm

70. Under "General Considerations," p. 392, the causes of death for the remaining 19 patients are reviewed; 5 of the 42 who had no operation recovered.

was placed against the trunk, the exit wound for one of the two matched a third entrance wound in the left side of the chest. The bullet entering there broke the lower margin of the tenth rib, passed through the diaphragm, spleen and left kidney and entered the aorta.

A few hours after the shooting the left leg became paralyzed, and severe pain occurred throughout the left foot. The bullet was removed from the left femoral artery by Dr. Karl Meyer. It had lodged near the groin, and the peritoneal cavity was not entered in the process of removing the bullet. Laparotomy was not performed. Gangrene of the left lower extremity was followed by amputation of that extremity. Death occurred four days after entrance. At the necropsy 732 Gm. of blood was found in the left pleural cavity; only 24 Gm. was present in the abdomen. The entrance wound in the aorta was 8 mm. in diameter and had inverted edges; it was located 4 mm. cephalad to the mouth of the left renal artery. Just to the right of the mouth of the celiac axis the aorta bore a triangular tear 12 by 3 mm., with everted edges. The periaortic fat there was intact. There were no clots in or about the aortic wounds. In the periaortic fat from the seventh thoracic vertebra down and about all the abdominal portion of the aorta there was a marked retroperitoneal hemorrhage. That the patient lived four days with such wounds in the aorta was as astounding as the migration path of the bullet.

Rubesch [71] found accounts in medical literature of the migration of missiles in the heart and blood vessels in 16 persons; to these reports he added 1. In 4 patients migration was from the heart. In one of these, his own patient, the bullet lodged in the right femoral artery; amputation was followed by recovery. In 3 other patients the passage of the missile probably occurred post mortem. Eleven patients who had no operations and 3 who had, all died; 4 recovered.

In our series bullet wounds of the aorta were found after death in the bodies of 7 patients who had not undergone laparotomy and in 2 of those who had; these last died on the operating table, the 7 who had not undergone laparotomy died from fifteen minutes to one hour after entrance except the patient with the bullet lodged in the femoral artery, who lived four days. Momm [72] reported the occurrence of a death twenty-seven days after the abdomen was wounded by a bullet which injured the liver and aorta. On account of a massive hemorrhage in the abdomen the wound in the liver was packed. Gangrene of the left leg developed; about a week before death an aneurysm of the left femoral artery in the groin was opened and the bullet was found between

71. Rubesch, R.: Ein Beitrag zur embolischen Verschleppung von Projektilen, Beitr. z. klin. Chir. **60**:394, 1912.

72. Momm: Ein Schuss durch Leber und Aorta, Tod nach vier Wochen infolge Sepsis, Deutsche med. Wchnschr. **36**:2242, 1910.

the artery and vein where pulsation had so pounded the bullet against the artery that the wall was torn for a length of 3 cm. After death a hole 7 by 3 mm. in diameter was found in the front wall of the aorta, 12.5 cm. above its bifurcation. On the opposite side was a hole 6 mm. in diameter through only the intima and media.

Without describing the entrance wound in the aorta, Kratter [73] has registered migration in the aorta of a bullet to a straddlewise lodging at the aortic bifurcation, obstruction of the left common iliac artery, gangrene of the left leg, amputation, death from uremia and ascending inflammation of the urinary organs in a woman who attempted suicide; laparotomy disclosed no visceral injury; death occurred two months after the shooting. Brentano [74] had a patient who lived for one week with two holes in the aorta where a 7 mm. bullet had passed from left to right close to the mouth of the superior mesenteric artery, its path being completely retroperitoneal. The review by Perthes [75] of the older literature includes 7 cases in which patients lived for from six to sixty days after sustaining bullet wounds of the aorta, one in which the patient lived for seven weeks and that of his own patient, who lived two hundred and ninety-five days.

CONCLUSIONS

The introduction of laparotomy for bullet wounds of the abdomen is definitely an American contribution to surgery, particularly by surgeons of the southern states.

Perhaps the most important element aiding the recovery of patients with bullet wounds of the abdomen is a short interval between the injury and the operation. This was recognized many years ago, and the discovery initiated a mortality rate that has not been appreciably changed since. It is common knowledge, however, that the publication of recoveries has met with more favor than that of deaths, whether the reports concern 1 or many patients.

The experience surgeons have had in dealing with this type of injury undoubtedly is a helpful factor.

Drainage after laparotomy for bullet wounds apparently is unimportant.

Bullet wounds of the abdomen in peace time occur especially in persons in the third decade of life: in the period of youth and daring.

Bullets entering the front of the abdomen cause more deaths than those entering the back; those entering the sides cause most deaths.

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73. Kratter: Seltene Schussverletzungen, Vrtljschr. f. gerichtl. Med. **31**:342, 1906.

74. Brentano: Schussverletzung der Aorta, Verhandlung d. deutsch Gesellsch. f. Chir. **33**:92, 1904.

75. Perthes, G.: Schussverletzung der Arteria pulmonalis und Aorta, Beitr. z. klin. Chir. **19**:414, 1897.

Thoraco-abdominal and abdominothoracic wounds are associated with a high mortality rate.

Overlooked wounds also play a large part in the mortality. Unfortunately, however, their influence is malign and the study of their importance has been neglected.

Patients who die of bullet wounds in the first twenty-four hours after injury die of hemorrhage and shock; when death occurs after twenty-four hours it is usually due to generalized peritonitis.

In only a few patients do the wounds require resection of viscera or parts of viscera.

CIRRHOSIS OF THE LIVER

WITH SPECIAL REFERENCE TO THE SURGICAL ASPECTS

EARL CLIFFORD HENRIKSON, M.D.
MINNEAPOLIS

Laënnec, in 1819, was the first to describe adequately and to name portal cirrhosis. Since his time hundreds of papers have been written, and many types of cirrhosis have been described. The following classification used in this study is taken from Bell's "Text-book of Pathology":

1. Portal cirrhosis (Laënnec's cirrhosis, atrophic cirrhosis, hobnail liver or gin-drinkers' liver)
2. Obstructive biliary cirrhosis
3. Pigmentary cirrhosis (hemochromatosis; bronze diabetes)
4. Syphilitic cirrhosis

Before discussion of the treatment of cirrhosis of the liver, which for years has been directed mainly toward relief of the ascites associated with the condition, the etiology, diagnosis, symptoms, physical findings, postmortem observations and causes of death will be considerd.

ETIOLOGY

The etiology of cirrhosis is obscure. The importance of alcohol as a factor becomes less and less convincing as the results of postmortem examination in large series of patients dying of alcoholism are studied. There was a history of the use of alcohol to some extent in 50 per cent of the cases considered in this paper. In many of the hospital records there is no indication whether the patient was asked about the use of alcohol. Many patients known to use liquor refuse to admit it. These facts are offset by the impression that an equally high percentage of patients with no cirrhosis will admit the use of alcohol. Formad observed cirrhosis at only 6 of 250 autopsies performed on chronic drunkards. However, the marked decrease after 1916 in the number of patients admitted to hospitals with a condition diagnosed as portal cirrhosis would seem to prove some association. To illustrate, the statistics compiled from the records of the Minneapolis General Hos-

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From the Minneapolis General Hospital and the Department of Surgery of the University of Minnesota.

Submitted to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of the requirements for the degree of Master of Science in Surgery.

pital and the Cook County Hospital are shown graphically (fig. 1). The number of cases before 1916 was high. The sharp decline in the incidence began a year earlier in Minneapolis than in Chicago. A study of the death rate in the registration area of the continental United States also gives the impression that the use of liquor is a factor in the production of the disease. In figure 2 is shown the decrease in the number of deaths due to cirrhosis after state and federal prohibition laws went into effect. A graph based on the figures obtained from Stockholm, Sweden, is shown for comparison. The great difference

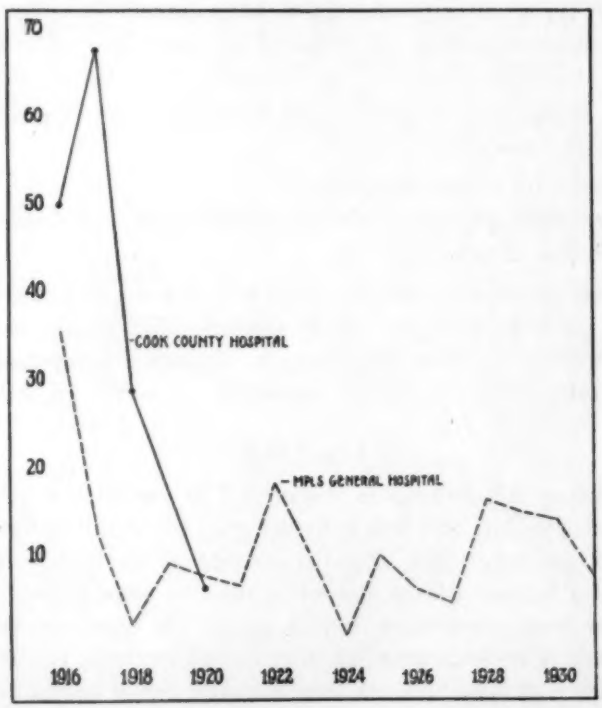

Fig. 1.—Graphs showing the number of patients per ten thousand of the population discharged who had a condition diagnosed as cirrhosis of the liver from the Minneapolis General Hospital from 1916 to 1932 and from the Cook County Hospital from 1916 to 1920.

between the curve for Minnesota (largely rural) and those for such states as New York and California (largely urban) may be due to the infrequency of diagnosis in rural districts or to the greater frequency of the condition in the urban population. Differences in diet, drinking habits and disease may be factors.

O'Malley stated that in certain classes of Orientals who never use alcohol but do use spices and other stimulating articles in their diet

cirrhosis of the liver is common. This observation adds weight to the theory that the disease may have a gastro-intestinal origin. One such hypothesis is that portal cirrhosis is caused by toxins or toxin-producing agents brought to the liver by the portal system and that if these toxins are carried by the arteries the disease may resemble the biliary types. Italian pathologists incline to the opinion that toxins arising in the spleen induce the disorder. Other foreign investigators believe that malaria is a factor, but few, if any Americans accept the malarial variety. Cirrhosis has been produced experimentally in animals by chloroform or a similar agent combined with bacterial infection and also by repeated injections of egg white or other protein to produce

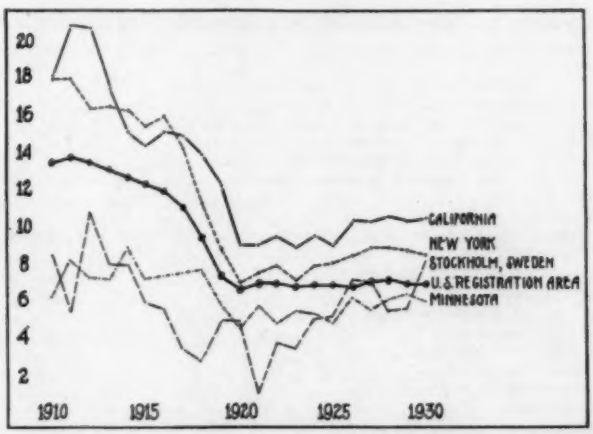

Fig. 2.—Graph showing the death rate due to cirrhosis of the liver per hundred thousand of the estimated population of the registration area of the United States from 1910 to 1930. The other graphs indicate that the diagnosis is made much more frequently in California and New York than in Minnesota. A graph constructed from the statistics obtained from Stockholm, Sweden, shows the same general trend as those for the three states selected as samples.

anaphylactic shock. Arsenic and copper are often accused. Hard liquors are said to be more likely than wine and beer to cause the condition. It would be interesting to know definitely whether there is any relationship to the use of alcoholic drinks before or after meals and whether the liver protected by the previous ingestion of carbohydrates is as readily injured as one not so protected. The coexistence of cirrhosis and diabetes, as in cases of bronze diabetes, at first thought seems to indicate that carbohydrates are of no value. However, in such cases diabetes may be superimposed on cirrhosis already well under way, or the same process may involve not only the liver and spleen but the pancreas.

DIAGNOSIS

The main object of the study reported here was to show what results can be expected from the surgical treatment of cirrhosis of the liver. In order to do this the literature on the subject was studied, and the records were reviewed of cases in the Minneapolis General Hospital and the University of Minnesota General Hospitals in which a diagnosis of cirrhosis had been made. Several of the charts recorded the diagnosis of Banti's disease or splenic anemia in addition to that of cirrhosis.

Of the 241 cases listed as instances of cirrhosis of the liver, 5 were included instead with those of splenic anemia, and 64 were excluded

TABLE 1.—*Summary of Cases in Which the Diagnosis Was Cirrhosis of the Liver* **

		Number
Cases in which the diagnosis was cirrhosis		241
Excluded to be classified as cases of splenic anemia		5
Excluded after inspection of liver at autopsy	5	
Excluded after examination of microscopic sections	5	10
Excluded because the diagnosis was questionable		64
Total cases excluded		79
Cases remaining for study		162
Cases in which the probable diagnosis was cirrhosis though not verified at autopsy or by biopsy		78
Cases in which the diagnosis was certain		84
Verified at autopsy		67
Verified at operation and by biopsy		17
Diagnosis made clinically		49
Diagnosis not made clinically		35
Patients known to be alive		3
Patients known to be dead		80
Condition unknown		1
Cases in which operation was performed		31
Talma-Morison (omentopexy, epiplopexy)		9
Talma-Morison and splenectomy		4
Splenectomy		4
Exploratory operation*		10
Cholecystotomy*		1
Cholecystogastrostomy*		1
Cholecystoduodenostomy*		1
Ventral herniotomy*		1

* The diagnosis of cirrhosis of the liver was not made until at operation or autopsy in most of these cases.

because the diagnosis was questionable owing to the presence of cardiac or renal disease, ulcers or congenital hemolytic icterus (table 1). That the symptoms in cases of cirrhosis may closely simulate those of these conditions will be seen from a study of the symptoms and findings given later. Cases were therefore probably excluded which rightfully should not have been. In 5 of 10 other cases which were excluded the clinical diagnosis was not confirmed on gross examination at autopsy, and 5 in which the diagnosis based on the gross appearance at postmortem examination was cirrhosis were excluded after microscopic examination by Dr. J. S. McCartney of the department of pathology of the University of Minnesota. He has recently completed a study of the

microscopic sections of the liver in about 300 cases of cirrhosis, taken from the autopsy material of that department. He examined the sections available in the series of cases considered in this paper. Seventy-eight of the 162 remaining cases were classified as instances of probable cirrhosis. While the symptoms and physical findings in these cases were typical, the liver was not examined, either grossly or microscopically, to confirm the diagnosis. In 84 cases the diagnosis of cirrhosis was verified. In 67 of the latter cases the diagnosis was verified by a study of autopsy material, and in 17 by examination or biopsy at operation. In only 3 of the 84 proved cases are the patients known to be alive; the condition of 1 patient is unknown, and the rest are dead.

An examination of table 2 shows that of the group of proved cases 64 were classed as instances of portal cirrhosis; 7, of the obstructive

TABLE 2.—*Distribution of Cases of Cirrhosis*

	Proved Cirrhosis	Probable Cirrhosis	Proved and Probable Cirrhosis
Number of cases	84	78	162
Types of cirrhosis (based on clinical diagnosis)			
Portal	64	48	112
Biliary (obstructive)	7	3	10
Syphilitic	7	8	15
Undefined	6	19	25
Sex			
Men	61	63	124
Women	23	15	38
Average age, years	47.5	52.1	49.5
Men	49.2	51.9	50.5
Women	40.9	52.7	45.1

biliary type, and 7, of the syphilitic type, while in 6 instances the diagnosis of cirrhosis was unqualified. The distribution according to these types was 48, 3, 8 and 19, respectively, for the group of probable or clinical cases. In 49 of the 84 proved cases the diagnosis was made clinically.

The diagnosis of cirrhosis of the liver is not always easily made, and in a few cases, as has just been mentioned, even gross examination of the liver may be misleading. Without question, many cases are reported in the literature as instances of cirrhosis in which the diagnosis would not be confirmed if sections of the liver were examined microscopically. If results obtained with the various types of treatment are to be compared to determine which method is the best, only cases proved to be instances of cirrhosis at autopsy or by biopsy should be included in the study. From the tables included in this paper a comparison can be made between the proved and the probable cases. The diagnosis in all cases in which it was not verified by autopsy or biopsy is based on the symptoms, physical and laboratory findings and apparent cause of death.

SEX AND AGE

As can be seen from table 2, cases occurring in men predominate in the proportion of about 3:1. The average age for both sexes is 49.5. The average age of the men is 50.5, and that of the women, 45.1. In figure 3 is shown the number of patients for each five year period of life. The disease is most common in the fourth and fifth decades.

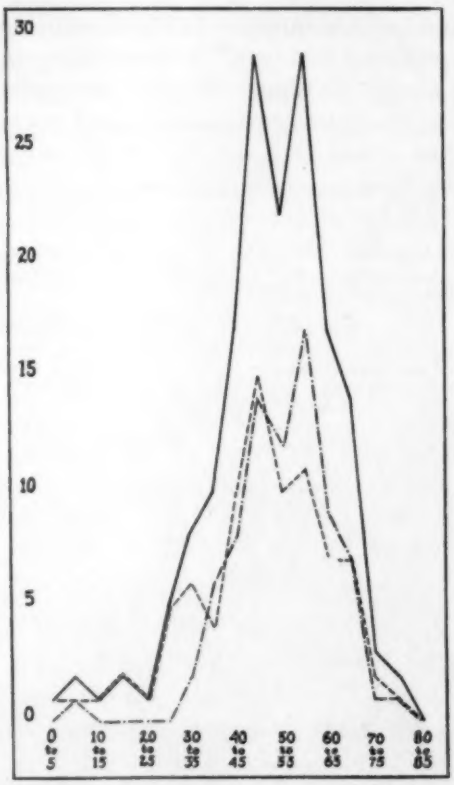

Fig. 3.—Graphs showing the distribution of cases according to age. In this figure the values for patients with proved cirrhosis are shown by short dashes; those for patients with probable cirrhosis, by a line of dots and dashes, and those for all patients by a solid line.

SYMPTOMS

Table 3 shows that the most common single complaint was that of abdominal distention (in 101 of 162 cases). It was usually due to ascites, but it may also be caused by an enlarged liver or spleen or by gaseous distention of the intestines.

In a study of 5,000 cases of ascites Cabot found that a correct diagnosis was made in only 39 per cent. The following causes were given in the order of their frequency: cardiac involvement, 1,397 cases;

renal damage, 665; cirrhosis, 325; tuberculous peritonitis, 263; ovarian and uterine tumors, 118; abdominal carcinoma, 109, and intestinal obstruction, 86. In 7 per cent of these cases ascites observed at autopsy proved to be due to cirrhosis of the liver. Some investigators believe that in most cases ascites associated with cirrhosis is caused by tuberculous peritonitis. Tuberculosis may be an incidental observation, however.

A commonly considered cause of ascites is obstruction of the portal circulation, resulting from contraction of fibrous tissue about the blood vessels or from portal thrombosis, which is frequently found associated with cirrhosis and especially with splenic anemia. Warthin expressed the belief that splenomegaly and the symptoms of Banti's disease are all due to primary infective thrombophlebitis of the portal or splenic veins and that when the condition is present in the portal trunk ascites develops, while if the splenic vein is blocked hematemesis may result from the rupture of dilated branches of the gastric veins. When the superior mesenteric veins are occluded pain, vomiting and diarrhea develop, and the patient collapses. Against the view that the fibrotic liver causes the obstruction are the many recorded cases of cirrhosis in which death occurred without ascites (65.6 per cent of a series of 56 cases reported by Lange at Kiel, Prussia, in 1888). A well established collateral circulation may have been present in many of these cases. In spite of the fact that ascites is the most common finding in cases of portal thrombosis (40 of 61 instances collected by Rolleston), the observation that the portal vein may be ligated in animals without the production of ascites is against the theory of portal obstruction as a common cause. Furthermore, in cases of thrombosis of the portal vein immediate effusion into the peritoneal cavity does not always take place, according to Ketchen. Then, too, in cases of atrophic cirrhosis considerable pressure on the portal vein exists before ascites supervenes. This is shown by the fact that hemorrhages occur long before fluid is present. If the fluid were a transudate from the blood vessels, the effusion would pass into the bowel and stomach and not into the peritoneal cavity, as it is in the mucous membranes rather than in the peritoneum that increased blood pressure resulting from occlusion of the portal vein produces the most marked engorgement.

Other theories attribute the ascites to the secretory activity of the endothelium, to increased inflow of lymph, to increased permeability of the walls of the blood vessels due to congestion or inflammation, to decreased outflow from the peritoneal cavity because of the obliteration of efferent vessels or to the decreased absorptive power of the endothelium and blood vessels, such as is seen in cases of chronic passive congestion. Cardiac failure may be important in some cases; chronic

peritonitis, in others. One of the more likely theories is that which explains the ascites as due to the circulation of toxins which the liver is unable to handle as a result of the great changes in it. This theory is favored by the presence of edema prior to the ascites. These toxins are said to arise from both the gastro-intestinal tract and the spleen. The latter organ may enlarge enormously and be responsible for as much as 50 per cent of the blood passing through the portal vein.

If one considers as most likely the theory that ascites is due to a combination of toxemia and portal obstruction, any operative procedure should aim (1) to relieve portal obstruction, as by the establishment of a collateral circulation; (2) to aid the liver in dealing more satisfactorily with the toxins, as by lessening the portal congestion and increasing the arterial supply to the hepatic cells, thus allowing hyper-

TABLE 3.—*Frequency of Occurrence of Symptoms in 162 Cases of Cirrhosis*

Symptoms	Proved Cirrhosis	Probable Cirrhosis	Proved and Probable Cirrhosis
Gastro-intestinal	65	61	126
Abdominal pain or distress	37	44	81
Nausea and vomiting	23	21	44
Constipation	12	18	30
Anorexia	19	19	38
Hematemesis	20	18	38
Bloody or tarry stools	16	11	27
Diarrhea	9	9	18
Clay-colored stools	4	4	8
Abdominal distention	45	56	101
Weakness	30	31	61
Loss of weight	26	30	56
Swelling of the feet	27	28	55
Dyspnea	24	30	54
Nocturia	22	26	48
Jaundice	26	21	47
Cough	9	12	21

plasia to take place, and (3) to remove the source of toxins when possible. If the spleen really is such a source, splenectomy would be of benefit, not alone because a source of toxins is eliminated but because the portal trunk is relieved of from 20 to 50 per cent of its venous blood supply.

Gastro-intestinal symptoms, present in 126 of 162 cases, may all be more or less dependent on the stasis in the portal vein. Hematemesis (present in 38 of 162 cases) may be due to (1) ulceration and rupture of dilated vessels at the lower end of the esophagus, (2) erosions and necrosis of the mucosa as a result of infective processes or (3) congestion of the gastric mucosa. In a study of 411 cases of gastro-intestinal hemorrhage Rivers, at the Mayo Clinic, determined that in 90 per cent the hemorrhage was due to intrinsic gastroduodenal lesions, such as peptic ulcer (in 78 per cent) and carcinoma of the stomach (in 7.8 per cent). Extrinsic lesions, such as cirrhosis of the liver (in 2.8 per cent) and splenic anemia (in 2.8 per cent) were responsible for the hemorrhage in 10 per cent of the cases. In respect to the two con-

ditions last mentioned, while splenomegaly itself may be a factor, the fact that hemorrhages do not occur frequently in other diseases in which splenomegaly occurs is against such a view. The hemorrhages may be explained as due to obstruction of the venous outflow from the spleen and the intestinal tract as a result of the accompanying hepatic cirrhosis or thrombosis of the splenic vein. Against the theory that infective thrombophlebitis is responsible for the hemorrhages is the absence of abnormalities in the vein at autopsy in most instances.

Abdominal pain and distress, complained of by 50 per cent of the patients in this study, in the cases of severe involvement may be due to occlusion of the mesenteric vessels. Symptoms of intestinal infarction may accompany the pain. In cases of less severe cirrhosis the pain may be due to intermittent claudication of the vessel. A few patients have had several attacks. Perisplenitis is usually responsible for the pain in the upper left quadrant.

According to Hollins, ascites alone is a frequent cause of anorexia, vomiting and diarrhea. However, the close relationship of the enlarged spleen and the stomach and the consequent dragging of the spleen on the fundus may be a factor. Splenectomy would, of course, be expected to benefit a patient with such symptoms.

Jaundice and clay-colored stools (observed in 8 cases) are most frequently seen in cases of the obstructive biliary type of cirrhosis. However, at times operation has been performed to relieve the obstruction and the operator has been chagrined to note that the ducts were patent. In such cases the liver is usually atrophic and fibrotic. In this series 86 of 162 patients (53 per cent) had jaundice, as determined by the physical findings, history and icteric index. Of the proved cases jaundice was present in 12 but the change in color had not been noticed. Eleven patients who complained of jaundice showed it on physical examination. Fourteen stated that they had been yellow at one time, but no evidence was found at the time of admission. Besides these 37 patients, 8 had neither a history of icterus nor a trace of it on physical examination, but the icteric index was 10 units or above.[1] Of the 78 probable cases jaundice was observed in 18, but it had not been noticed. Seven patients gave a history of jaundice but did not have icterus on physical examination at the hospital. Thirteen complained of being yellow and were found to be so on examination. Three not complaining of jaundice or revealing it on physical examination had an icteric index of 10 or above. Thus, in 45 per cent of the proved cases and in 41 per cent of the probable cases, or in 53 per cent of the total number, jaundice was present during the course of the disease.

1. The normal range is from 4 to 6 units. In clinical icterus the index is above 15. The range for latent jaundice is from 6 to 16 units.

Weakness (in 61 of 162 cases), dyspnea (in 54 of 162 cases), debility, palpitation and irregularities of menstruation may be explained on the basis of anemia and less often on that of cardiac involvement. Loss of weight (in 56 of 162 cases) may be dependent on the gastrointestinal symptoms, but Hollins, who expressed the belief that Bacillus coli is the cause of splenic anemia (Adami suggested it as a cause of hepatic cirrhosis), considered the wasting to be a result of the effect of toxins on the central nervous system. He stated that there is vasomotor paresis of the splanchnic area. Hebetude, nervousness, restlessness and insomnia, which were rare in this series, are attributed to toxemia due to a poorly functioning liver.

TABLE 4.—*Frequency of Occurrence of Physical Findings in 162 Cases of Cirrhosis*

	Proved Cirrhosis	Probable Cirrhosis	Proved and Probable Cirrhosis
Abdominal distention	65	56	121
Ascites	57	52	109
Palpable liver	53	48	101
Cardiac murmur	39	40	79
Edema	38	33	71
Jaundice	22	32	54
Abdominal varices	21	27	48
Palpable spleen	23	24	47
Enlarged heart	29	17	46
Hernia	14	12	26
Dyspnea	13	10	23
Cyanosis	16	7	23
Hemorrhoids	5	6	11
Blood pressure, average	118 systolic, 73 diastolic	123 systolic, 75 diastolic	120 systolic, 74 diastolic
Systolic, above 140	9 of 70	11 of 57	20 of 127
Systolic, below 120	40 of 70	21 of 57	61 of 127

PHYSICAL FINDINGS

The most common physical finding is ascites (observed in 121 of the 162 cases, table 4). This condition has already been considered in detail. A palpable liver, present in 101 cases, was the next most frequent finding. Some investigators consider hypertrophy of the liver as merely one stage of cirrhosis, while others differentiate the atrophic and the hypertrophic type. A palpable spleen was found in 47 of the 162 cases. The enlargement may be due to obstruction of the hepatic and portal circulation or to the fact that the spleen is equally involved by the process producing the disease picture. The symptom complex known as Banti's disease may represent one extreme of a pathologic process which at one time affects the liver more severely and at another the spleen.

Cardiac murmur, which occurred in a large number (79) of the 162 cases in this series, edema (in 71), cardiac enlargement (in 46) and cyanosis (in 23) may serve to confuse the diagnosis of cirrhosis

with that of diseases of the heart. Autopsy in 7 cases revealed valvular disease; in 1, chronic myocarditis, and in 8, coronary sclerosis.

The blood pressure is usually low. The average pressure was 118 systolic and 73 diastolic in the proved cases and 123 systolic and 75 diastolic in the probable cases. The average pressure for both groups was 120 systolic and 74 diastolic. While hypertension was present in a few cases, in more than one-half the blood pressure was below the general average. Rest in bed and the general debility associated with the disease are influential factors.

TABLE 5.—*Laboratory Findings in Cases of Cirrhosis**

	Proved Cirrhosis	Probable Cirrhosis	Proved and Probable Cirrhosis
Blood			
Hemoglobin, average percentage	71	73	72
Below 70	32 of 80	20 of 72	52 of 152
Above 90	6 of 80	6 of 72	12 of 152
Erythrocytes, average	3,798,000	3,831,000	3,800,000
Below 3,000,000	13 of 75	10 of 64	23 of 139
Above 4,500,000	4 of 75	16 of 64	20 of 139
Leukocytes, average	6,380	6,060	6,220
Below 7,000	32 of 55	33 of 58	65 of 113
Urea nitrogen, mg. (average for 56 cases)	25.4	19	23
Wassermann reaction (108 cases)			
Positive	8	10	18
Negative	49	34	83
Positive and negative	5	2	7
Urine (151 cases)			
Albumin	35	36	71
Casts	24	27	51
Sugar	4	6	10
Bilirubin	20 of 26 tested	9 of 15 tested	29 of 41 tested
Urobilin	11 of 21 tested	16 of 22 tested	27 of 43 tested
Urobilinogen	4 of 15 tested	9 of 15 tested	13 of 30 tested
Contents of stomach			
Free hydrochloric acid	11 of 21*	18 of 24†	29 of 45
No free hydrochloric acid	10 of 21	6 of 24	16 of 45
Character of stools			
Clay-colored	5	7	12
No bile	4 other cases	1	5
Tarry	4 other cases	3	7
Bloody (red)	2 other cases	3	5
Occult blood	7 other cases	7	14

* Unless otherwise specified, the figures in the columns represent numbers of cases.
† The average value for free hydrochloric acid for the group with proved cirrhosis was 19 degrees; for the group with probable cirrhosis, 28 degrees.

LABORATORY FINDINGS

A tendency to anemia and leukopenia is indicated by an average hemoglobin content of 72 per cent and an average erythrocyte count of 3,800,000 (table 5). Readings vary with the technician and the instrument used. The table shows the number of hemoglobin readings below 70 or above 90 for each group and also the number of patients with a red cell count below 3,000,000 or above 4,500,000. The average white cell count in all cases was 8,440. In the cases classified as probable instances the average count was 7,450, and in the proved cases, 9,260. When cases of leukocytosis apparently due to inflammation, such as pneumonia and peritonitis, were omitted, the average count was 6,220,

the count in the probable cases being 6,060 and that in the proved cases, 6,380. The count was below 7,000 in 65 of 113 cases (57 per cent).

The urea nitrogen content of the blood averaged 19.4 mg. for 23 probable cases and 25.4 mg. for 35 proved cases. The average for 58 cases of the two groups in which it was determined was 23 mg. In 16 cases in which an operation was performed the urea nitrogen content ranged from 2.4 to 101 mg. (table 5). The patient with a content of 2.4 mg. died on the second day after an operation for a ventral hernia. The patient with the reading of 101 mg. had had a value of 35 mg. a short time previously. She died about one and one-half years after a Talma-Morison procedure.

Tests of hepatic function were performed in only a small percentage of the cases in this series. The pheno-tetra-chlorphthalein test was usually employed, and in 16 of 19 tests impaired function was demonstrated. Rowntree found some degree of retention of bromsulphalein in 80 of 87 patients in his series of 112. Barker expressed the belief that the rose bengal test is the best. The normal person retains 50 per cent of this dye for the first eight minutes and 25 per cent for sixteen minutes, while the person with cirrhosis retains from 65 to 85 per cent for eight minutes and from 40 to 75 per cent for sixteen minutes.

The results of Wassermann tests of the blood, urinalyses, Ewald tests, fractional determinations and analyses of the stools are shown in table 5.

The ascitic fluid in a typical case of cirrhosis is clear and yellowish or greenish and may have a specific gravity as high as 1.015; it contains as much as 0.4 per cent albumin. More albumin is present in cases of cirrhosis than in those of renal ascites and less than in those of cardiac and tuberculous ascites. In the latter condition the specific gravity is about 1.020; the fluid is turbid, and the predominating cell type is the lymphocyte. In cirrhosis the endothelial cell predominates. The presence of polymorphonuclear leukocytes indicates peritonitis.

OBSERVATIONS AT AUTOPSY

Autopsy was performed on 67 of the patients in this series. The spleen was removed at operation in 8 cases. The data were incomplete in a few instances. The average weight of 61 livers was 1,760 Gm. (A liver weighing 525 Gm. from a child 8 years old and another weighing 625 Gm. from a child 1 year old are not included.) The usual normal limits for the weight of the liver of an adult ranged from 1,300 to 1,800 Gm. The largest liver in this series weighed 3,200 Gm. Four weighed more than 3,000 Gm. Twenty-one weighed more than 2,000 Gm. The smallest liver weighed 550 Gm.; 26 weighed less than 1,500 Gm., and 9 less than 1,000 Gm.

The average weight of the spleen obtained at autopsy or by splenectomy in 64 cases was 400 Gm. (This does not include a spleen weighing 250 Gm. from the 8 year old child or one weighing 150 Gm. from the 1 year old child.) The average weight of the spleen for normal adults is 150 Gm. The largest spleen weighed 1,735 Gm.; 41 weighed more than 300 Gm., and 14 weighed 500 Gm. or more.

The gallbladder was pathologic in 11 instances. Eight patients had coronary disease; 7, valvular disease, and 1, chronic myocarditis. Esophageal varices were definite in 11 cases. In many instances, owing to collapse of the walls, the varices are not observed unless the pathologist distends them by the injection of fluid.

CAUSES OF DEATH

The most common cause of death was hepatic insufficiency, 18 patients dying in coma. Some other causes of death were hemorrhage with hematemesis occurring near the time of death in 14 patients, peritonitis in 8, bronchopneumonia in 8 and chronic alcoholism in 5. Six patients died within a day or two after operation. Obstructive jaundice and chronic pancreatitis were each present in 4 cases. Thrombosis of the portal vein and nephritis were stated as the cause of death in 3 instances each.

TREATMENT OF CIRRHOSIS OF THE LIVER

MEDICAL MANAGEMENT

Support for the rigid dietary regimen enforced on patients with cirrhosis of the liver appears evident from the experiments of Bollman. He has demonstrated the protective value of carbohydrates in instances of cirrhosis of the liver in dogs. Cirrhosis was produced by the oral administration of 5 cc. of carbon tetra-chloride two or three times a week for about two years. More recently, 1 cc. of tetra-chlorethane, which is present in a substance used during the World War to waterproof the fabric in airplanes, has been employed. The dogs kept on a diet high in carbohydrates (chiefly milk and corn syrup) were little affected by the administration of these toxic substances, while those maintained on a diet of meat frequently showed symptoms of profound toxemia. Lesions produced in the liver were less severe in the first group, and the repair was much more rapid. Almost perfect repair occurred in several dogs receiving over two hundred doses of carbon tetra-chloride.

Ascites was produced experimentally in dogs with obstructive jaundice of several months' duration. In the dogs maintained on a diet high in carbohydrates marked ascites developed about twenty-four hours after meat was fed. A small amount of meat extract produced

ascites in a few hours. With further repetition of the injury to the liver with carbon tetra-chloride ascites developed which could not be controlled by diet.

Hepatic insufficiency is treated by pushing the administration of carbohydrates intravenously and orally. Digestive disturbances should be treated symptomatically. Complications are treated as they arise. Mercury and iodides may be tried, but if improvement results the possibility of wrong diagnosis presents itself. For itching Rowntree advised from ¼ or ½ grain (16.2 or 32.4 mg.) to as high as 2 grains (129.6 mg.) of mild mercurous chloride daily for three or four days at a time. Sweating may bring relief.

The dietary restrictions usually observed are as follows: Alcohol, eggs, spices, condiments and fats are forbidden. The staple article of diet should be milk. This is supplemented by vegetables, cooked fruits, cereals and bread. Meats are allowed only occasionally.

To deplete the circulation mild saline cathartics, such as solutions of sodium phosphate, magnesium citrate and magnesium sulfate, are said to be useful. Blum, Aubel and Hausknecht described 3 cases in which calcium chloride with restriction of salt (sodium chloride) was used with good results. The dose is from 11.1 to 22 Gm. by mouth for from five to six days at intervals of from eight to ten days. The calcium is eliminated by the bowel; the chlorine, by the kidney. As the chlorine is freed from the calcium it is forced to combine with the sodium, and the sodium is eliminated and with it the surplus of water. Further work with calcium chloride has been done by Mejebovskiy, who studied 11 patients on a diet of baked potatoes, rice cooked without salt, boiled meat, fruit and eggs. One or two glasses of weak tea were allowed daily. For two or three weeks from 12 to 15 Gm. of calcium chloride was given daily, and this was well tolerated. The results were positive in 8 cases and negative in 2, and the degree of ascites remained stationary in 1 instance. Recurrences developed in 6 cases after from three to eleven months. In 1 case the amount of urine increased fourfold. The sodium chloride content increased notably in the urine and blood. One patient lost 15 Kg. in weight in three weeks. The ascites disappeared. The loss of weight was not associated with diuresis, since the intake of fluid was 500 cc., and the output of urine, only 400 cc. Calcium chloride would seem, then, to promote extrarenal elimination. The theory is that the action is due to colloidal changes. Excessive changes in the tissue colloids, such as those due to anemia, may explain failures in the treatment of some patients. Mejebovskiy expressed the belief that the stasis in the portal system is primary and that the physiochemical changes in the colloids of the endothelium of the vessels and in those of the peritoneum are other factors. The chlorine anion plays the funda-

mental rôle, and the calcium cation, the secondary rôle. The effect of the calcium chloride is present only when the food is free from salt; otherwise, this medication may favor the accumulation of fluid.

Careful attention must be paid to elimination, both through the urinary tract and by way of the alimentary canal. As regards the use of diuretics, Beckman in his "Treatment in General Practice" stated: "It is generally agreed that all the older diuretics nearly always fail to reduce ascites of hepatic origin. Regarding novasurol (merbaphen) it may be said that the majority of the clinicians in Germany, where the drug originated, have been of the opinion that it too was of no avail in these cases." (Brunn, Mühling and Hassencamp were quoted.) Bleyer reported good results in 1 case. Fodor maintained that the drug is effective provided the patient has normal blood pressure. In the United States Rowntree, Keith and Barrier stoutly championed its use in connection, it should be noted, with their combination of a low fluid intake, a diet low in salt and the administration of ammonium chloride. They obtained good results in 10 cases, with disappearance of both the ascites and the signs of collateral circulation. The patients improved markedly in health and strength. Chapman stated that jaundice, persistent bleeding from the gastro-intestinal tract and mental disturbances contraindicate the use of diuretics in most instances. Elderly cachectic patients with poor hepatic function may be made definitely worse by their use. In 1930 Rowntree, from an analysis of cases observed during an experience of six years with the use of merbaphen, found that 75 and 85 per cent of the patients in 2 series were benefited by the use of the drug. He stated that the average duration of life after the development of ascites in cases of cirrhosis was found by White and Thompson to be two months, while in his own series of 28 living patients it was 38.4 months. However, 54 per cent of the patients had died within sixteen months, even if the condition was controlled. Eighty-four of the 112 patients who died had lived for an average of fifteen and nine-tenths months. He stressed the importance of early diagnosis and early operation. While the immediate results were good in 80 per cent of the cases in which treatment was medical, 75 per cent of the patients died within six years.

Follow-up letters sent to the patients treated medically at the University of Minnesota and Minneapolis General Hospitals revealed that only a small number could be traced, owing to the time elapsed since the patients were hospitalized and to the roving spirit of patients of the type seen in general hospitals. One patient (J.T.) is still living nineteen years after symptoms began. He returned to the hospital after receiving his follow-up letter and was admitted for study because of pain in the right upper quadrant and marked distention of the abdomen.

A test of liver function showed fairly marked damage to the liver. The gaseous distention was relieved by the use of salts and enemas, and he left the hospital much improved. One patient is living after thirteen years, but is anemic. Three patients died thirteen years after symptoms began. One of the latter persons was troubled with edema and bloating during the last years of his life. A fourth patient, who had had symptoms for twelve years, died three years after leaving the hospital. He was tapped sixteen times at home. One patient died of hemorrhage in the Minnesota General Hospital eight years after the onset of symptoms. He stated that soon after the symptoms began he was tapped at the Mayo Clinic and was sent home to die, but instead he did hard labor for eight years to within about ten days of his death. One patient is alive and in fair health after seven and one-half years, but he is anemic and jaundiced and complains of swelling of the abdomen and feet. Two others died seven and six years, respectively, after their symptoms began. A woman, six years after the onset of symptoms, is bedridden and edematous and vomits material containing blood. A patient who became ill five years ago is now in fair health, except for anemia. One man died three years after the onset of symptoms. Another died two and three-fourths years after symptoms began. He was always jaundiced and had melena at times. He vomited blood the day he died. The diagnosis of cirrhosis was confirmed at autopsy. One patient died after two and a half years of illness. One patient who has lived two years is troubled by abdominal pain and enlargement, and 2 who have lived more than two years complain of weakness. One died at the Mayo Clinic a short time after leaving the Minneapolis General Hospital. He lived two years after the onset. Four others died two years after the first symptoms appeared; 1, fourteen months; 1, six, and 1, five. A patient recently discharged from the hospital is living five months after the onset of illness.

A summary shows, then, that only 9 patients treated medically, and hence classified as probably having cirrhosis, are known to be alive. They are still living nineteen, thirteen, seven and one-half, six, five, two, two and two years and five months, respectively, after the onset of symptoms.

A general study of the records of all the patients who were not treated surgically shows that the duration of life in the group of proved cases was shorter than that in the group of probable cases (table 6). In the former group 100 per cent of the patients died within eleven years, as compared with 67.3 per cent of those in the latter group. At the end of six years the percentages were 93 and 53, respectively. The average for the two groups after six years was 72.6 per cent. In Rowntree's series of patients treated medically, 75 per cent were dead within six years (table 12).

The difference between the group of proved cases and the group of probable cases may be due to the fact that most of the patients with proved cirrhosis entered the hospital in poor condition and died there, while most of those with probable cirrhosis entered and left the hospital in fair condition. Then, too, in the latter group are included those on whom an autopsy was not permitted. Hence, in spite of the typical symptoms and physical findings, these patients may not have had true cirrhosis. The difficulty of diagnosis, even at autopsy, is demonstrated by the necessity of excluding several cases from this study when microscopic examination failed to confirm the diagnosis made from the gross specimen. Studies of series of cases in which the diagnosis of cirrhosis

TABLE 6.—*Comparison of Mortality Rates in the Different Groups*

Duration of Symptoms, Years	Unproved Cirrhosis: (A) Group in Which Treatment Was Medical (49 Cases), Percentage	(B) Average for Groups A and C (95 Cases), Percentage	Proved Cirrhosis	
			(C) Group in Which Treatment Was Medical (46 Cases), Percentage	(D) Group in Which Treatment Was Surgical (31 Cases), Percentage
1	22.0	41.0	60.0	45.1
2	32.6	48.0	65.2	54.8
3	51.0	62.0	76.0	58.0
4	53.0	67.5	82.5	64.6
5	53.0	69.4	86.9	64.6
6	53.0	72.6	93.0	67.4
7	57.1	75.0	95.6	70.0
8	63.2	78.9	97.8	74.1
9	65.3	81.0	97.8	80.6
10	65.3	81.0	97.8	80.6
11	67.3	83.1	100.0	87.0
12	67.3	83.1	....	87.0
13	69.3	84.2		
14	75.5	87.0		
15	75.5	87.0		
16	77.5	88.3		
17	77.5	88.3		
18	79.5	89.3		
19	79.5	89.3		
20	79.5	89.3		
21	82.2	90.4		

was based only on symptoms and physical findings cannot be considered trustworthy. Diagnosis based on inspection and palpation of the liver is usually correct, but if the gross specimen is not typically hobnailed, examination of sections under the microscope is essential for positive diagnosis.

Of interest in this summary of the results is the fact that the patients subjected to surgical treatment had lived, even before the operation, over twice as long after the onset of symptoms as had, on the average, the patients not operated on. Patients in the latter group died in an average of eighteen and three-tenths months after the onset of symptoms, while those of the former had had symptoms for an average of thirty-nine months before operation. The average duration of life after operation was five months, thus bringing the total duration of life after the onset of symptoms to an average of forty-four months. This

value is high because of the fairly large percentage of patients who were known to have had the disease for between five and ten years. The course of the disease in these patients, then, was slow, and little credit can be given to surgical intervention for the fact that the patients submitting to operation lived longer on the average than those treated medically.

Of further interest is the finding that the patients lived on the average over a year after the onset of ascites. This value compares favorably with an average period of sixteen months given by Chapman, Snell and Rowntree, from whose paper table 7 is taken. These authors had 28 patients who lived for an average of over thirty-eight months. Forty patients lived or were living longer than the average of sixteen months. Credit for this increase in the length of life after the development of ascites is attributed by the last-mentioned authors in

TABLE 7.—*Expectancy of Life After Onset of Ascites as Given by Various Authors* *

Author	Number of Cases	Average Duration of Life After Onset of Ascites, Months
Thacher	7	1.3
Nissen	26 (paracentesis)	1.5
	25 (no paracentesis)	1.0
White	12 (paracentesis)	2.1
	10 (no paracentesis)	2.0
Flint	16	5.0
Ramsbottom	31	6.0
Chapman et al	112	16.0
Henriksson	42	12.8

* This table was taken in part from the article by Chapman, Snell and Rowntree, 1931.

part to improved methods of treatment. However, that not all the credit should be given to any type of medical management for the apparently better prognosis after the development of ascites is brought out by the finding that of the 42 patients in my series on whom the study was complete and who lived for an average of twelve and eight-tenths months after ascites began, only 2 were given merbaphen, 1 ammonium chloride and mersalyl, 1 aminophylline and 2 magnesium sulfate. The intake of fluids was restricted for 6 patients, and a light diet was ordered for 5. Seventeen patients of the series underwent operation. The question then arises whether the ascites is now recognized earlier both by the patient and by the physician or whether the course of the disease is becoming less progressive. The patients reported on by Chapman, Snell and Rowntree were seen within the last ten years, and those in my series within the last fifteen years. The other authors cited in table 7 reported their findings between 1893 and 1920. Does the Eighteenth Amendment or the section of the country play a part in this difference? Studies of series published elsewhere in the future will help to answer these questions.

SURGICAL INTERVENTION

PALLIATIVE MEASURES

Paracentesis.—Mild peritonitis may play a rôle here. Cures result from the collateral circulation established by adhesions.

OPERATIVE TREATMENT

Historical Survey.—The caput medusae perhaps first directed attention to nature's attempt to establish a collateral circulation in cases of cirrhosis of the liver. In a postmortem study on persons who had met death by accident Fagge demonstrated that many persons with typical cirrhosis of the liver were in good health, owing to the establishment of a compensatory circulation. While he was not the first to show this, his careful and scientific observations were instrumental in placing the subject on a sound basis. Talma of Utrecht, Netherlands, in 1887 or 1888, suggested that an attempt should be made to develop a collateral circulation by the establishment of adhesions between the parietal and the visceral peritoneum. Van der Meulen attempted to do this for Talma in 1888, but the patient died of shock in a few hours. Talma published nothing on the subject until 1898. Lens, of Netherlands, performed a successful operation in 1891, after which the patient lived six months. This case was not reported until 1901. A patient of Schley died of peritonitis after operation in 1891. Unaware of the work of these men, Morison, of Newcastle, England, on the suggestion of Drummond, performed an omentopexy in 1894. The patient was not cured but lived eighteen months. A short time later another patient was operated on with successful outcome. These cases were reported in the first article ever written on the subject in 1896. Other surgeons performing the operation before the close of the century were: Howard, 1897; Neuman, of Berlin, 1898; Weir, of New York, 1898; Turner, 1899, and Brown, 1899.

Selection of Patients for Operation.—There is marked diversity of opinion as to what constitutes indications and contraindications for operation on patients with ascites. Morison stated that alcoholic cirrhosis is most readily cured and that he has seen no cures in cases of syphilitic cirrhosis. Turner agreed that patients with syphilis do badly, while Murrell recommended treating the syphilis medically three weeks and then, if there is no improvement, operating as in other cases. Barker reported good results after surgical intervention in such cases. White and Thompson advised against operation in cases in which ascites is due to cirrhosis alone, as patients with such a condition hardly ever survive even a tapping for more than a few weeks. It is their contention that cure results from operation only in the cases in which there is chronic peritonitis, which in turn is the cause of the ascites. Lejars expressed a view that every patient with chronic ascites is benefited by

laparotomy. In the cases in which ascites is due to portal cirrhosis operation must be performed early, before the liver is too seriously involved. He stated that it has long been known that patients with tuberculous peritonitis often recover after simple laparotomy. He added that even those with generalized carcinosis survive longer and in comparative comfort when simple drainage under aseptic conditions has been attempted. Murrell cited carcinoma as a contraindication, and Wheeler stated that among the patients unsuited for operation are those with ascites due to other causes than cirrhosis of the liver. Talma himself listed the following contraindications to operation: (1) a high grade disturbance of the function of the liver, (2) icterus, (3) xanthoma and (4) pruritus. It was his practice always to tap the patient twice to note the effect before operating. White added diabetes, Bright's disease, mental hebetude, pronounced acholia and urobilinuria to the list of contraindications. He agreed with Talma that operation is contraindicated if the patient has not withstood several tappings. On the other hand, Allyn stated that repeated tappings and edema of the feet seem to make no difference in the prognosis but that hebetude, nervousness, restlessness or insomnia is an unfavorable symptom, because it indicates toxemia. Most surgeons require that sufficient parenchyma of the liver be present to carry on the hepatic functions. Schiassi observed the excretion of urea to gain information on the condition of the hepatic cells. O'Malley expressed the belief that operation should be deferred in cases of acute peritonitis and also in instances in which paracentesis shows turbid or heavy ascitic fluid or fluid with a high content of albumin. He deferred operation, too, if there was pleural effusion, abdominal pain or elevation of temperature. Furthermore, he added glycosuria to albuminuria and urobilinuria as symptoms of poor prognostic import. From a study of their own cases Eliot and Colp concluded that as regards prognosis the patients offering the most favorable prognosis are those between the second and the fourth decade of life, who are fairly well nourished, and without severe nephritis, cardiac lesions or signs of collateral circulation, who have withstood a few tappings, in whom the disease has come on gradually during a year or more, whose liver is of the hypertrophic type and on whom the Schiassi type of omentopexy has been performed with local anesthesia.

Rowntree divided cirrhosis into the types in which there is compensation of the liver and those in which there is decompensation. He stressed the importance of early diagnosis and treatment. If operation is to be performed, it should be before decompensation takes place. From a study of 132 cases Greenough found that results were better in patients with an enlarged liver than in those with an atrophic liver, and that the presence of adhesions or perihepatitis was of good prognostic import.

In the series reported in this paper the results have no definite relationship to the size of the liver or the duration of the ascites. Nor is the duration of the disease of great significance. In one patient the disease may run a rapid course; in another, a slow course. Each patient selected for operation must be studied carefully. Hepatic function, not the size of the liver; the progress of the disease, not the duration, and the condition of the patient in general with special reference to that

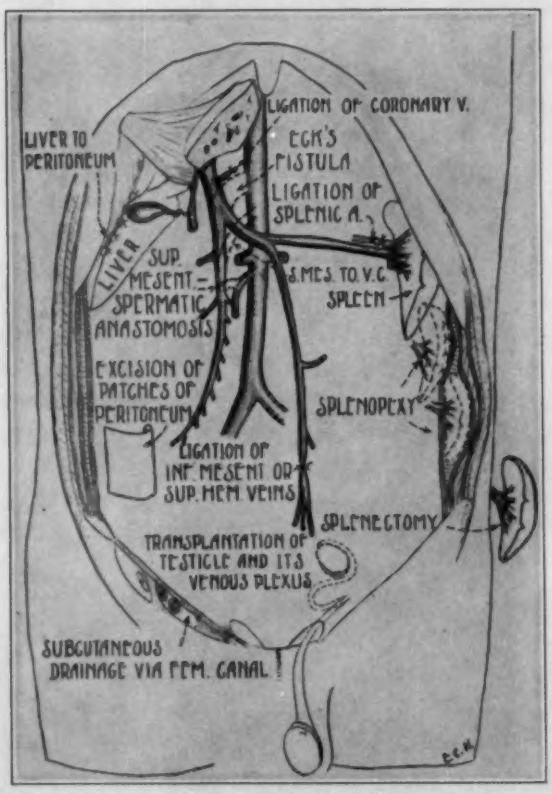

Fig. 4.—Composite drawing illustrating a few procedures which have been suggested in the surgical treatment of cirrhosis of the liver.

of the heart and kidney, not the age or the benefit derived from tapping, are of greatest significance.

In other words, before the patient is subjected to surgical intervention, it must be determined that he is a good surgical risk and that his condition is such that he has a good chance of improving should the operative procedure itself be successfully completed.

Procedures (figs. 4 and 5).—1. Methods of Establishing Collateral Circulation: (*A*) Omentopexy. Morison's procedure is to open the

abdomen above the umbilicus and empty it of fluid. The peritoneum covering the spleen and liver and the parietal peritoneum opposed to them are scrubbed with a dry gauze sponge. The omentum is sutured across the anterior part of the abdominal wall; a glass tube is left in the pouch of Douglas, and the parietal wound is closed, silk sutures being used. To keep the parietal and the visceral peritoneum in contact long circular strips of adhesive tape are wrapped about the patient's trunk

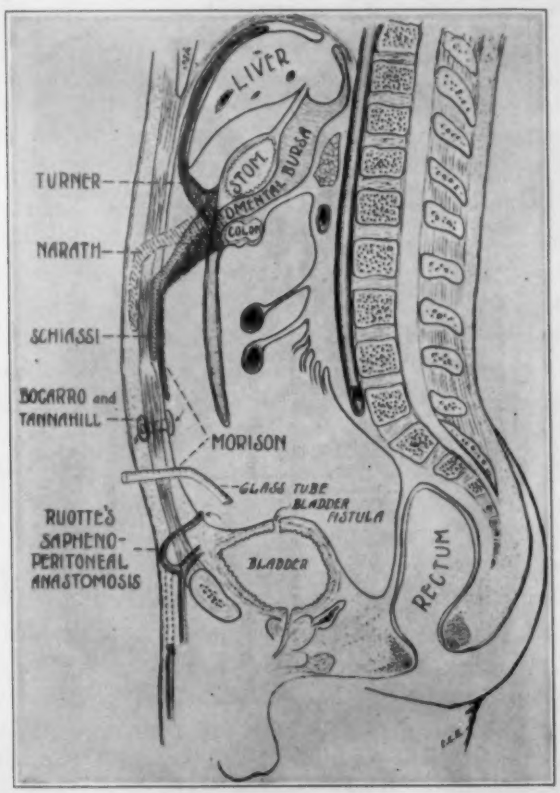

Fig. 5.—Drawing illustrating the various types of omentopexy and a few other procedures not indicated in figure 4.

from the epigastrium to the tube in the hypogastrium. There are many modifications of this operation. Few surgeons use drainage because of the danger of infection, although Morison stated that peritonitis had never developed in his cases. However, Greenough reported a mortality of 50 per cent in 54 cases in which drainage was used, as compared with that of 14 per cent in cases in which no drainage was employed. Turner interposed the omentum between the liver and the

diaphragm. Extraperitoneal fixation of the omentum has become popular. Both Schiassi and Barker placed the omentum in a pocket formed between the peritoneum and the posterior surface of the abdominal muscles. Narath brought out the omentum beyond the muscle beneath the skin and superficial fascia.

(*B*) Visceropexy. Hepatopexy is a possible method. Many surgeons as a routine fix the margin of the liver to the peritoneum by a few sutures. Others excoriate the surface to encourage the formation of adhesions.

Splenopexy was mentioned by Bunge at the Surgical Congress in 1902. By some surgeons the spleen if small is brought out into pockets in the abdominal wall, and if large it is merely sutured to the incision.

Lanz, in 1911, transplanted the testicle and spermatic cord to the peritoneal cavity and surrounded them with omentum.

Excision of patches of peritoneum has also been recommended as a means of producing collateral circulation through the adhesions thus formed.

(*C*) Ligation of vessels. To hasten the formation of the collateral circulation, ligation of the chief tributaries of the portal vein is carried out at times. Moynihan ligates the inferior mesenteric vein. Mayo ligates the inferior mesenteric or superior rectal vessels as a supplement to epiplopexy.

2. Operations in Which a Short Circuit is Effected: To relieve the liver of some of the blood entering from the portal system, Vidal made an Eck fistula, after which the patient lived three months.

Although often accomplished, anastomosis of the superior mesenteric and spermatic or ovarian veins has not given encouraging results. However, Bogoraz and Krestovsky reported good results after anastomosing the superior mesenteric vein and the inferior vena cava.

It must be remembered that the liver should not be deprived of too much blood, as such symptoms as convulsions, delirium and coma are said to have resulted when this happened. As shown by Pearson, studies on dogs by Hahn, Pawlaw, Massen and Wencki helped to demonstrate this danger.

3. Methods Used for Drainage of Ascitic Fluid: Ruotte's saphenoperitoneal anastomosis has given good results in almost 50 per cent of the cases (Griffith). Handley employed the femoral canal for subcutaneous drainage. Bocarro and Tannahill reported good results from the use of glass tubes resembling collar buttons which drained into the subcutaneous tissues. For the same purpose, other surgeons use silk threads, rubber tubes or sections of blood vessels, but occlusion or obliteration soon takes place.

TABLE 8.—*Duration of Life After Operation*

Author Reporting	Operation and Present Status of Patient	Less Than 1 Mo.	Less Than 6 Mo.	6 mo. to 1 Yr.	1 to 2 Yr.	2 to 3 Yr.	3 to 4 Yr.	4 to 5 Yr.	5 to 6 Yr.	6 to 7 Yr.	7 to 8 Yr.	8 to 9 Yr.	9 to 10 Yr.	10to 11 Yr.	11 to 12 Yr.	12 to 13 Yr.	Died or ?	Improvement	No Improvement	"Cured"
White, S., 1906 (227 cases)	Epiplopexy	..	..	7	7	17	5	..	..	..	..	..	..	..	..	..	75 33%	29 13%	34 15%	84 37%
	Hypertrophic circulation 24																			
	Cured 10																			
	Improved 6																			
	Not improved 3																			
	Dead 5																			
	Atrophic circulation 84																			
	Cured 38																			
	Improved 7																			
	Not improved 10																			
	Dead 27																			
Turner, 1906, 1909 Morison, 1912	Morison procedure																			
	Dead	6	1	..	1	1	..	..	..	1	..	..	..	..	..	..	..	..	..	..
	Alive and well	..	..	1	1	2	1	..	..	..	..	..	..	..	..	1	..	..	5	1
Weber, 1909																				
	Alive; ascites	..	..	..	..	..	1	..	..	..	..	(1 other recovery)				..	..	..	..	1
Ricketts, 1909	Omentopexy																			
	Dead	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	Alive and well	..	..	..	1	..	.	..	..	..	..	..	..	..	..	..	..	..	1	..
Sherren, 1909	Narath																			
	Alive and well	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	1	..
Brown, 1909	Talma-Morison																			
	Alive and well	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..
Eliot, 1910	Modified Talma																			
	Alive and well	..	..	..	..	..	..	1	1	..	..	(4 others cured)				..	..	..	2	4
Woolse, 1910	Talma																			
	Alive and well	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	1	..
Dock, 1910	Talma-Morison																			
	Died postoperatively	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	Omentopexy																			
	Alive and well	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	1	..
Wilkie, 1911	Talma-Morison-Narath																			
	Alive and well	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	1	..
Van der Veer, 1912	Morison																			
	Died after operation	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	Alive	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	2	..
Smith	Splenectomy	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
King, 1919																				
	Alive and well	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	1	..
Eliot and Colp, 1919	Omentopexy																			
	Dead	8	2	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	Alive	..	3	2	2	..	..	..	..	..	..	..	..	..	..	..	..	..	7	..
	Lost track of	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	5	..	..
Potter	Talma-Morison																			
	Alive	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..

Potter	Lost track of	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	5	..	..
	Talma-Morison																				
	Alive	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..

Griffith, 1921	Ruotte																				
	Dead	..	5	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	Alive	..	..	..	..	1	1	..	1	..	..	(34 others)			..	..	..	..	20%	22%	
Birt	Splenectomy																				
	Alive	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	1	
Bocarro, 1922	Button drain																				
	Alive and well	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	
Gibbon and Flick, 1922	Omentopexy																				
	Alive	..	..	2	1	..	..	..	1	..	..	..	..	..	..	..	..	..	2	2	
	Dead	2	2	..	..	..	1	1	..	..	..	..	..	..	..	..	..	..	..	..	
Mayo, 1924	Talma-Morison																				
	Dead 7	..	7	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Alive 21	..	..	..	..	..	..	..	1	..	1	1	1	(17 others)			..	..	..	..	
	Splenectomy																				
	Dead 7	..	7	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Alive 28	..	..	..	..	..	..	..	4	..	2	..	2	(19 others)			..	..	..	..	
	Splenectomy and Talma-Morison																				
	Dead 2	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Alive 7	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
Lester, 1926	Narath																				
	Alive	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	
Tempsky, 1926 (25 cases)	Talma																				
	Dead 6	5	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	5	..	
	Alive 19	..	..	1	1	1	1	1	..	..	..	..	..	..	1	..	..	6	13	..	
Hughson, 1927 (26 cases)	Modified Talma, 19; laparotomy, 3; splenectomy, 1; etc.																				
	Dead	17	..	7	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Alive	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
Tannahill, 1930	Epiplopexy and buttons 1																				
	Alive	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	
Bernheim	Ruotte																				
	Dead	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	
Henrikson, 1933 (31 collected cases)	Talma-Morison 9																				
	Dead	2	3	2	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Alive	1?	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Talma-Morison and splenectomy 4																				
	Dead	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Alive	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Splenectomy 4																				
	Dead	2	1	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Cholecystogastrostomy 1																				
	Dead	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Cholecystostomy 1																				
	Dead	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Cholecystoduodenostomy 1																				
	Dead	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Exploratory operation 10																				
	Dead	6	1	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Alive	..	..	1	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	
	Ventral herniotomy 1																				
	Dead	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	

Paracentesis or continuous external drainage, with rubber or glass drains, is sometimes used.

The establishment of a sinus into the bladder has been attempted.

4. Splenectomy: Gerster and Hartman ligated the splenic artery to produce atrophy of the spleen.

An unsuccessful case of splenectomy was reported by Rafferty as early as 1900. Results obtained by Mayo since then would indicate that this procedure is exceedingly helpful in many cases.

Splenectomy with a modified Talma procedure seems to be gaining favor.

5. Other Procedures: According to Rowntree, hemorrhage due to rupture of esophageal varices accounts for a large number of deaths in cases of cirrhosis of the liver. He suggested that the collateral circulation be blocked by ligation or injection, so as to preclude the possibility of the portal blood reaching the esophageal varices. This was done by Walters in a patient, aged 61, whose stools contained blood daily. His procedure was total division of the gastrohepatic omentum, mass ligature of the divided ends and incorporation of the ends into the abdominal incision. After operation no blood was present in the stools.

Injection of sclerosing solutions into the esophageal varices via the esophagoscope has been considered.

Operations, such as cholecystostomy and cholecystenterostomy, are performed in cases in which obstructive symptoms obtain.

Diathermy to produce hyperemia has been tried over the liver with benefit.

Results of Surgical Treatment (tables 8 and 9).—It has been said that statistics concerned with the value of surgical procedures are unreliable, because few men report unfavorable results while most hasten to report favorable results. With regard to results in the surgical treatment of ascites this tendency is more than offset by the fact that so many poor results that are published are due to the operation having been performed as a last resort, when little or no benefit could be expected from any treatment. Then, too, operations which were devised primarily for the relief of portal cirrhosis are employed in many cases in which the diagnosis is anything but that. Authors favoring operation in cases of portal cirrhosis state that this accounts for many poor results, while those opposed to surgical intervention claim that the reported cures occur in cases in which the diagnosis was obscure. Cumston cited Willems as admitting only 10 favorable results in 250 cases reported by the Germans. Most statistics show improvement in about 50 per cent after operation. Of 47 patients operated on at the Mayo Clinic, 7 died in the hospital; 21 were alive when last heard from,

1 being alive nine years after operation, 1 eight years after; 1 more than seven years after and 1 more than five years after. In an editorial in the *American Journal of Surgery,* June 1909, the following results in 1,565 cases in which omentopexy had been performed were given: (1) patients cured, 30.4 per cent; (2) patients relieved, 19.8 per cent; (3) patients not relieved, 39.2 per cent, and (4) patients dying, 10.6 per cent. In other words, 50.2 per cent were benefited, and 49.8 per cent were not. In a series of 207 cases (included in table 8) selected at random from the reports of 27 authors published since 1909, improvement was noted in 65 per cent and no benefit in 35 per cent. Omentopexy was performed in 108 of these cases, with improvement in 67 and none in 41 (table 9). Splenectomy was performed in 55 cases, with improvement in 45 and none in 10. Saphenoperitoneal anastomosis gave relief in 20 of 42 cases, while in 22 there was no improvement. Button

TABLE 9.—*Summary of Results of Several Surgical Procedures*

	Improvement		No Improvement or Patient Dead	
	Number of Cases	Percentage	Number of Cases	Percentage
Ruotte's saphenoperitoneal anastomosis	20	47.6	22	52.4
Omentopexy	67	62.0	41	38.0
Splenectomy	45	81.8	10	18.2
Button drains	2	100.0		
	134	65.0	73	35.0

drains were used in 2 cases, with improvement in both instances. While the latter series is far from complete, the results in the last half of the period of forty years during which operations have been performed in cases of cirrhosis with ascites indicate an improvement in 65 per cent of the cases in which surgical intervention was used, or in 15 per cent more than in the first half, during which improvement occurred in 50.2 per cent. The most striking results were those of Mayo who obtained improvement in 24 of 28 cases in which omentopexy was performed and in 27 of 34 cases of splenectomy, while the poorest results were those reported by Tempsky, only 7 of 25 patients showing improvement.

The following results were obtained from operations performed on patients in this series:

1. Of 9 patients on whom a Talma-Morison procedure or omentopexy was performed, 8 died in one, eleven, thirty-nine, one hundred and one, one hundred and eighty-three, one hundred and eighty-four, three hundred and sixty-five and five hundred and forty-seven days after operation; 1 left the hospital in good condition after an operation in 1914 and has since been lost track of.

2. Of 4 patients on whom a Talma-Morison procedure and a splenectomy [2] were performed, 1 died one hour after operation and 2 on the sixth day after operation; 1 is alive and well three and one-half years after operation.

3. Four patients on whom splenectomy [2] only was performed died two, nineteen, one hundred and forty and six hundred and seventy-one days after operation.

4. Nine of the 10 patients on whom exploratory operation only was done died in one day, fourteen days, nineteen days, twenty-three days, twenty-seven days, thirty days, six months, four years and four and one-half years after operation; 1 is living eight and one-half months after operation.

5. One patient undergoing cholecystogastrostomy lived only one day.

TABLE 10.—*Duration of Life After Operation*

Type of Operation	Condition of Patient	Less Than 6 Mos.	6 Mos. to 1 Yr.	1 to 2 Yrs.	2 to 3 Yrs.	3 to 4 Yrs.	4 to 5 Yrs.	Total Number Patients
Talma-Morison	Dead	5	2	1	1	..	..	9
	Alive	1?						
Talma-Morison and splenectomy	Dead	3	..	..	..	..	..	3
	Alive	..	..	..	..	1?	..	1
Splenectomy	Dead	3	..	1	..	..	..	4
Cholecystogastrostomy	Dead	1	..	..	..	..	..	1
Cholecystotomy	Dead	1	..	..	..	..	..	1
Cholecystoduodenostomy	Dead	1	..	..	..	..	..	1
Exploratory operation	Dead	6	1	..	..	..	1	8
	Alive	..	1	..	..	..	1	2
Ventral herniotomy	Dead	1	..	..	..	..	..	1
Summary	Dead	21	3	2	1	..	1	
	Alive	..	1	..	..	1?	1	
	No trace	1	..	..	..	..	..	
		22	4	2	1	1?	2	31

6. One patient on whom cholecystotomy was performed died three months after operation.

7. One patient on whom cholecystoduodenostomy was performed died of peritonitis on the ninth day.

8. One patient died two days after ventral herniotomy.

A study of this summary and of tables 10 and 11 reveals that in this small series of 31 patients undergoing some type of operation, including exploratory laparotomy and herniotomy, 17 (55 per cent) died within thirty days of the operation. Twenty-one (67.7 per cent)

2. Since these figures were made up, 4 more patients have been operated on at the Minneapolis General Hospital for the relief of cirrhosis. The following results were obtained: C.C.—Talma-Morison procedure and splenectomy—died two days later; F.W.—splenectomy—died one day later; G.P.—Talma-Morison procedure and splenectomy—died one day later; A.J.—excision of patch of peritoneum followed in one month by splenectomy—died four days later.

died within six months, and 25 (77.4 per cent), within the first year. Operation was apparently a last resort for 5 patients, who underwent surgical treatment ten, ten, eight, eight and seven years, respectively, after the onset of symptoms. These 5 persons lived eleven, two, one hundred and eighty-three, nine and five days, respectively, after operation.

TABLE 11.—*Summary of Data on Patients on Whom Operation Was Performed*

No.	Age, Yrs.	Duration of Symptoms Before Operation	Urea Nitrogen of Blood, Mg.	Size of Liver or Weight in Gm.	Duration of Ascites	Operation	Duration of Life After Operation
1	67	1 mo.	....	3,180	1 mo.	Talma-Morison	1 day
2	45	10 yrs.	....	1,560	2 wks.	Talma-Morison	11 days
3	44	8 yrs.	8.9	3,080	2 wks.	Talma-Morison	6 mos.
4	57	9 mos.	....	Palpable	.....	Talma-Morison	101 days
5	27	7 yrs.	....	1,400	.....	Talma-Morison	5 days
6	23	8 mos.	18.6	2,725	6 wks.	Talma-Morison	183 days
7	51	9 mos.	....	Palpable	9 mos.	Talma-Morison	39 days
8	40	11 days	....	Palpable	11 days	Talma-Morison	Alive†
9	35	6 yrs.	35.0 101.0	1,200	5 yrs.	Talma-Morison	547 days
10	38	1 yr.	....	Palpable	4 mos.	Talma-Morison and splenectomy	1 hr.
11	57	18 mos.	11.2	Palpable	18 mos.	Talma-Morison and splenectomy	7 days
12	41	5 yrs.	....	Palpable	5 yrs.	Talma-Morison and splenectomy	3½ yrs.*
13	8	2 mos.	21.0	525‡	2 mos.	Talma-Morison and splenectomy	6 days
14	42	6 mos.	....	Not palpable	6 mos.	Splenectomy	19 days
15	26	10 yrs.	....	2,100	.....	Splenectomy	2 days
16	18	2 wks.	11.2	1,450	.....	Splenectomy	11 mos.
17	31	6 wks.	26.3	950	2 wks.	Splenectomy	140 days
18	51	2 yrs.	14.0	Palpable	.....	Cholecystotomy	3 mos.
19	34	6 wks.	....	Palpable	.....	Cholecystogastrostomy	1 day
20	46	8 yrs.	19.6	2,360	.....	Cholecystoduodenostomy	9 days
21	50	9 mos.	2.4	2,370	.....	Ventral herniotomy	2 days
22	45	5 days	42.0	Not palpable	.....	Exploratory	1 day
23	31	1 mo.	....	3,140	.....	Exploratory	4½ yrs.
24	63	1 yr.	....	Palpable	.....	Exploratory	19 days
25	57	2 mos.	....	Palpable	1 mo.	Exploratory	23 days
26	48	4 mos.	....	Palpable	.....	Exploratory	4 yrs.*
27	49	3 wks.	9.1	Palpable	.....	Exploratory	2 wks.
28	18	4 mos.	15.0	Palpable	.....	Exploratory	8½ mos.*
29	47	8 wks.	23.3	Palpable	9 days	Exploratory	1 mo.
30	13	6 mos.	16.8	1,110‡	4 mos.	Exploratory	6 mos.
31	26	1 mo.	....	Not palpable	1 mo.	Exploratory	8 days

* Patient alive.
† Patient lost track of after leaving the hospital.
‡ Child.

One patient who had an exploratory operation four months after the symptoms began is alive and well four years after operation. Another operated on five years after the development of ascites is alive and well three and one-half years after omentopexy and splenectomy. A third patient is still living eight and one-half months after operation, and a fourth was lost track of after the operation.

Eight patients who were 50 or past lived one hundred and one, ninety, thirty-nine, twenty-three, nineteen, seven and two days and one day after operation. In general, the older patients did not do well.

PROGNOSIS

After careful analysis of the charts the following averages were obtained:

Duration of Life	Days	Months
After the onset of symptoms in 75 proved cases in which operations were or were not performed	663	22.1
After ascites developed in 42 cases	385	12.8
With no operation in 45 cases	554	18.3
After the onset of symptoms in 19 cases in which operation for cirrhosis was performed	1,324	44.1
Between the onset of symptoms and operation in 19 cases	1,178	39.2
After operation for cirrhosis in 19 cases	150	5

As has already been mentioned, these values show that the patients subjected to surgical treatment had lived even before operation, more than twice as long after the onset of symptoms as had, on the average, the patients on whom no operation was performed. Whether the patients would have lived for an average of five months longer without operation is difficult to state.

TABLE 12.—*Comparative Durations of Life After the Onset of Symptoms for Several Series of Patients with Cirrhosis*

	Patients Treated Surgically, Dying Within 6 Years, Percentage	Patients Not Treated Surgically,† Dying Within 6 Years, Percentage
Rowntree's series	66.0	75.0
My series	67.4*	72.5†
Nineteen other series	64.0	

* This series includes the patients on whom an operation, such as exploratory laparotomy, cholecystotomy, cholecystogastrostomy, etc., was performed, the conditions of most of whom had not been diagnosed as cirrhosis before operation.

† The value 72.5 per cent includes not only the patients treated medically but those who had no medical treatment, owing either to the lack of diagnosis or to the death of the patient soon after admission to the hospital before medical management could be instituted.

In tables 6 and 13 are shown the percentage and number, respectively, of the patients who died during each year after symptoms began. Of the 31 patients undergoing operation, 67.4 per cent died within six years of the onset of symptoms, while 72.5 per cent of those not operated on died within the same period. These statistics correspond closely to those reported by Rowntree (66 and 75 per cent) and to similar values computed on the basis of 108 cases reported in the literature by 19 authors (table 12).

These results are discouraging, to say the least. It is evident that the patient with cirrhosis is a poor surgical risk. With this in mind, the selection of the type of operation must be given serious consideration. Splenectomy or a modified Talma procedure with splenectomy would seem to offer the best possibilities (table 9), but the associated high mortality should make one hesitate to perform these operations on any but those who present the best risks.

Vascular anastomosis, such as Eck's fistula, is far too formidable a procedure for any one to attempt but the surgeon skilled in vascular

TABLE 13.—*Duration of Life After the Onset of Symptoms*

	No.	Less 6 mo. Than 6 Mo.	6 mo. to 1 Yr.	1 to 2 Yr.	2 to 3 Yr.	3 to 4 Yr.	4 to 5 Yr.	5 to 6 Yr.	6 to 7 Yr.	7 to 8 Yr.	8 to 9 Yr.	9 to 10 Yr.	10 to 11 Yr.	11 to 12 Yr.	12 to 13 Yr.	13 to 14 Yr.	14 to 15 Yr.	15 to 16 Yr.	16 to 17 Yr.	17 to 18 Yr.	18 to 19 Yr.	19 to 20 Yr.	20 to 21 Yr.	Total
Patients with probable cirrhosis	78																							
Dead	40	6	5	5	9	1	..	..	2	2	2	..	1	..	1	3	..	1	..	1	..	..	1	40
Alive	9																							
Improved		1	..	..	2	..	..	1	..	..	..	..	..	..	..	1	..	..	..	..	..	1	..	..	6
Not improved		..	..	..	1	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	3
No trace	20																							
Improved		5	1	4	2	..	2	2	2	..	..	..	..	..	1	1	..	..	..	..	..	..	..	21
Not improved		1	5	1	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	8
Patients with proved cirrhosis	84																							78
Treated medically	53																							
Alive	0																							
Dead	46	23	5	2	4	4	2	3	1	1	..	..	1	..	..	..	..	..	..	..	..	..	..	46
No history	7	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	7
Treated surgically	31																							
Alive	3	..	..	1	..	..	1	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	3
Dead	27	9	5	3	1	2	..	1	1	1	2	..	2	..	..	..	..	..	..	..	..	..	..	27
No trace	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Types of operations																								84
Talma-Morison	9																							
Dead		1	2	1	..	..	..	..	1	1	1	..	1	..	..	..	..	..	..	..	..	..	..	8
Alive		1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Talma-Morison and splenectomy	4																							
Dead		1	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	3
Alive		..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	1
Splenectomy	4																							
Dead		..	2	..	..	1	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	4
Cholecystogastrostomy	1																							
Dead		1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Cholecystotomy	1																							
Dead		..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Cholecystoduodenostomy	1																							
Dead		..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	1
Exploratory	10																							
Dead		6	..	..	..	1	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	8
Alive		..	..	1	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2
Ventral herniotomy	1																							
Dead		..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Summary of results for patients with proved cirrhosis treated medically and surgically		—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	31
		32	10	6	5	6	3	4	4	2	3	..	3	(7 with no history and 1 lost)										84

surgical technic. Apart from the technical difficulties, this procedure is not recommended for a carnivorous animal like man, because of the danger of flooding the body through the portal circulation with split products from the digestion of proteins.

For patients whose poor condition contraindicates a major procedure one or more of the minor procedures, such as the saphenoperitoneal anastomosis of Ruotte or the establishment of subcutaneous drainage with the use of small glass spools, would seem from reports in the literature to offer hope. Since these procedures aim only at the relief of ascites, however, they appear at best to be palliative. If the patient's condition should improve after the ascites has been controlled, the way would be paved for splenectomy, with or without omentopexy.

An attempt to shut off the venous supply to the lower esophageal vessels to prevent hemorrhage is hardly feasible when the attack is made from below the diaphragm. Bleeding from the many anastomosing branches above the diaphragm would still be a likelihood. Obliterating the lumen of the varices themselves by direct attack through the esophagoscope appears more logical.

SUMMARY AND CONCLUSIONS

1. While the etiology of cirrhosis is obscure, the most plausible theory is that portal cirrhosis is caused by toxins or toxin-producing agents brought to the liver by the portal system. (Toxins from the spleen must be considered.) Evidence points to the association of alcohol with the development of cirrhosis.

2. After cardiac and renal pathologic conditions have been ruled out as the underlying process, the clinical diagnosis of cirrhosis of the liver can be made with a fair degree of certainty for a patient, usually a man, in the fourth or fifth decade of life who complains of abdominal pain or distress, nausea and vomiting, constipation or diarrhea, anorexia, hematemesis or melena, associated with general malaise, edema, loss of weight, dyspnea, clinical or latent jaundice and nocturia. On examination he presents ascites, a cardiac murmur, edema, a tendency to jaundice, a palpable spleen, a finely nodular liver (after paracentesis) and often albumin and casts in the urine. The patient usually dies in coma or of hemorrhage or of an infective process.

3. In 84 cases in this series the diagnosis of cirrhosis was proved at autopsy or at operation and by aid of biopsy, and these cases are considered separately. For statistical accuracy only the proved cases should be included in studies of this disease.

4. In the medical or nonsurgical management of cirrhosis judicious selection of cases is essential. The best results were those reported by Chapman, Snell and Rowntree with the use of a special diet, a limited

intake of fluids, ammonium nitrate or ammonium chloride, merbaphen or mersalyl and at times the employment of purines as diuretics. Only carefully selected patients were treated. The average length of life after the onset of ascites for the patients in their series was sixteen months, while in 28 cases it was thirty-eight months, as compared with an average of twelve and eight-tenths months in the series reported in this paper, in which there was no special management. At the end of six years 75 per cent of the patients reported on by the aforementioned authors were dead, as compared with 72.6 per cent of the patients without surgical treatment in this series. The values were 93 and 53 per cent, respectively, for the two groups, of proved and probable cases (table 6).

5. In the selection of patients for operation a careful study of the liver, kidneys and heart should be made to determine (*a*) whether the patient is a good surgical risk and (*b*) whether he has a good chance of improving later should the operative procedure itself be successfully completed. Early diagnosis and early operation should improve the results.

6. The type of operation should depend on the condition of the patient. If he is a poor surgical risk, paracentesis may be the only procedure indicated. Other procedures for controlling the ascites, such as the use of collar-button-like tubes draining into the subcutaneous tissues and the saphenoperitoneal anastomosis of Ruotte, are reported as giving good results. The more formidable procedures attempting (*a*) to establish collateral circulation and (*b*) to decrease the volume of blood storming the harassed liver via the portal gate, such as the establishment of an Eck fistula, anastomosis of the superior mesenteric vein and the inferior vena cava, splenectomy, the Talma-Morison procedure or one of its modifications or a combination of omentopexy and splenectomy, are indicated only in especially selected, well prepared patients because of the associated high mortality rate.

7. The multiplicity of operative procedures devised for the relief of patients with cirrhosis indicates their inadequacy. The failure of some types to give relief can be explained by (*a*) the technical difficulties involved in carrying out the procedure, (*b*) the mechanical failure of the procedures even when properly performed and (*c*) their use as a last resort in patients who are poor risks, with the consequent high rate of mortality.

8. The results of surgical treatment reported in the literature vary widely, the most striking being those reported by Mayo, which indicated improvement in 24 of 28 cases in which omentopexy was performed and in 27 of 34 cases in which splenectomy was performed. The poorest results are those reported by Tempsky, which indicated improvement in only 7 to 25 cases. In a series of 250 cases Cumston cited Willems as admitting favorable results in only 10 cases.

9. In a series of 136 cases reported in the literature, death occurred in 52 per cent within one year of operation. Of my series of 19 patients operated on for cirrhosis, 67 per cent died within one year of operation, while 77.4 per cent of the 31 patients undergoing some type of operation, including such procedures as exploratory laparotomy or herniotomy, died within the same time. Over one-half the patients died within thirty days of operation. These statistics demonstrate the very high mortality rate among patients with cirrhosis.

10. Six years after the onset of symptoms 67.4 per cent of the 31 patients in this series undergoing some form of operation (table 12), 66 per cent of those in Rowntree's series and 64 per cent of those in a series of 108 cases (reported on by nineteen authors) were dead. Compared with values indicated in paragraph 4, these percentages indicate a preference for surgical treatment, were it not for the following facts: In the 19 cases just mentioned the average duration of life from the onset of symptoms to operation was thirty-nine months. The average duration of life after operation was five months, or a total of forty-four months from the onset of symptoms to death, as compared with an average of eighteen and three-tenths months for those whose treatment was medical. The patients undergoing operation had then (even before the operation) lived over twice as long as those without operation. Whether the average length of postoperative life of five months was an increase or a decrease in the expected duration of life is difficult to state.

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EFFECT OF REMOVAL OF STELLATE SYMPATHETIC GANGLION ON GROSS AND HISTOLOGIC STRUCTURE OF THE THYROID GLAND

AN EXPERIMENTAL STUDY

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Since Koeben [1] in 1855 first suggested the sympathetic origin of disease of the thyroid, numerous investigators have attempted to prove or to disprove his theory.

It has been demonstrated by Anderson,[2] Berkley [3] and Rhinehart [4] that the thyroid is amply supplied by nonmedullated nerves, ending in fine fibrils, with knoblike enlargements on the basal ends of the gland cells. Briau [5] has shown by anatomic and embryologic dissections that the thyroid nerves come from the cervical portion of the sympathetic trunk, arising in the main from the middle of the cervical portion of the trunk in man and from the inferior cervical or stellate ganglion in the dog and cat. It has also been demonstrated that ganglion cells exist both in the superior laryngeal nerves [6] and in the thyroid gland.[7]

In the attempt to demonstrate a functional relation between the thyroid and its nerve supply many conflicting reports of experimental studies have been made. These include various histologic changes after

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the administration of pilocarpine,[8] not confirmed by others;[9] both degeneration[10] and hyperactive changes[11] following stimulation of the sympathetic nerves (likewise contradicted by other findings[12]); histologic changes after division of the cervical sympathetic chain[13] and after division of the laryngeal nerves;[14] absence of histologic changes after bilateral removal of the laryngeal nerve,[15] and similarity of transplanted and intact thyroid glands.[16]

Great variations in the physiology of the gland, estimated by various procedures, have been reported. The thyroglobulin content of the thyroid has been observed to be increased following the injection of epinephrine.[17] The iodine content has been observed to be decreased[18] and unchanged[19] following the stimulation of the sympathetic trunk, while another investigator reported a decrease after the division of the cervical portion of the sympathetic trunk.[13b]

The conclusions cited previously regarding the histologic change in the thyroid after division of its sympathetic supply were based in some instances on observations on one or two animals. For that reason the problem was again undertaken, twenty dogs being used, all of which were studied under identical conditions. The operations were performed with strictly aseptic technic. Ether was used as the anesthetic, the neck was shaved and cleaned with iodine and alcohol, and a lobe of the

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thyroid gland or stellate ganglion was removed through a midline incision. In all the dogs the wounds healed per primam, and at the termination of the experiments specimens were first removed with the animals under anesthesia, and then the animals were killed. Specimens were immediately placed in solution of formaldehyde and Zenker's fixative and then stained with Weigert's hematoxylin and eosin.

TABLE 1.—*Comparison of Lobes of the Thyroid Gland of Dogs After Unilateral (Right) Lobectomy*

Dog	Time Between Operation and Death	Breed of Animal and Age	Hyperplasia		Round Cell Infiltration		Vascularity		Colloid		Comment
			L	R	L	R	L	R	L	R	
301	8 mo.	Fox-terrier, 6 to 7 yr.	+	++	+	+	+	++	+	+++	
317	18 days	Beagle, 10 mo.	+	++	+	+	+	+	++	++	
320	7 mo. 1 day	Police, 2 yr.	+	+	++	++	+	+	++++	+++	No striking differences between lobes
325	7 mo. 8 days	Fox-terrier, 2 yr.	+	++	+	+	+	+	++	+++	
334	3 mo. 23 days	Mongrel, 3 yr.	++	+	+	+	+	+	+	++	

TABLE 2.—*Comparison of Lobes of the Thyroid Gland in Dogs After Unilateral and Bilateral Stellate Ganglionectomy*

Dog	Time Between Operation and Death	Breed of Animal and Age	Hyperplasia		Round Cell Infiltration		Vascularity		Colloid		Comment
			L	R	L	R	L	R	L	R	
304	7 mo. 23 days	Mongrel, 2 to 3 yr.	+	+	+	+	+	+	+	+	Ganglionectomy on left; died of dysentery; postmortem changes in thyroid but no apparent difference
307	8 mo. 2 days	Mongrel, 6 mo.	+	+	+	+	+	+	++	++	Ganglionectomy on left
256	3 mo. 21 days	Mongrel, 1 to 2 yr.	+	+	+	+	+	+	+++	++	Bilateral ganglionectomy
321	7 mo.	Mongrel, 1 yr.	+++	+	+	+	+	+	+	+	Ganglionectomy on left
Puppy 1	23 days	Collie, 4 wk.	+++	+++	+	+	+	+	+	+	Ganglionectomy on left
Puppy 2	26 days	4 wk.	++	++	+	+	+	+	+++	+	Bilateral ganglionectomy

UNILATERAL LOBECTOMY OF THE THYROID

Several experiments were carried out to study the effect of unilateral lobectomy on the normal thyroid under conditions prevailing during this study. It was noted that the two lobes of the thyroid in the same animal were similar but that thyroids removed from different animals showed considerable variations (table 1). This was corroborated by the

studies of several investigators.[20] The fact that great differences exist between normal thyroids cannot be too strongly emphasized when one makes an appraisal of the results of an experiment of this kind.

UNILATERAL AND BILATERAL STELLATE GANGLIONECTOMY

In this series the left stellate ganglion was removed except in two animals, in which both ganglions were removed. The thyroid was not disturbed. Only animals exhibiting postoperative pupillary changes, enophthalmos and redundant conjunctiva were included in this series. Further proof that the cervical chain was removed was gained by microscopic examination. After varying periods of time we could find no definite changes in the thyroid glands which might serve to distinguish them from the lobes of thyroids removed in the first series (table 2).

TABLE 3.—*Comparison of Lobes of the Thyroid Gland of Dogs After Removal of the Right Lobe and the Left Stellate Ganglion*

Dog	Time Between Operation and Death	Animal and Age	Hyperplasia		Round Cell Infiltration		Vascularity		Colloid	
			L	R	L	R	L	R	L	R
303	1 mo.	Brown, 1 yr.	++	+	++	+	+	++	+	++
305	7 mo. 1 day	Black and tan, 2 yr.	+	++	+++	+	+	+	+	+++
318	7 mo. 1 day	Large brown, 4 to 5 yr.	+	+	+	+	+	+	++++	++
326	1 mo. 1 day	Brown mongrel, 9 mo.	+	+	+	+	++	+	+	+++
336	16 days	Mongrel, 1 yr.	+	+	+	+	+	++++	+++	++
358	3 mo. 23 days	Mongrel, 2 yr.	+	+	+	+	++	++	++	++

UNILATERAL LOBECTOMY AND GANGLIONECTOMY OF THE OPPOSITE SIDE

In this series the right lobe of the thyroid and the left stellate ganglion were removed at the same time. Again no changes could be seen in the remaining lobe of the thyroid which could honestly be said to distinguish it from the normal lobe (table 3).

CONCLUSIONS

1. The fact that in the normal dog there are wide variations in the histologic appearance of the thyroid gland is important in the appraisal of the results of an experiment of the kind described.

20. Fuhr, F.: Arch. f. exper. Path. u. Pharmakol. **21**:387, 1886. Halsted, W. S.: Tr. A. Am. Physicians **28**:127, 1913. Hunnicutt, J. A.: Am. J. M. Sc. **148**:207, 1914. Watts.[12e] Weiner.[13b] Rahe, Rogers and Fawcet.[18]

2. No definite changes could be demonstrated in the remaining lobe of the thyroid, using one lobe as a control, after (*a*) unilateral lobectomy, (*b*) cervical ganglionectomy and (*c*) unilateral lobectomy and simultaneous ganglionectomy on the opposite side.

PROTOCOLS

All operations were performed under sterile technic through a midline incision in the neck extending from the manubrium to the thyroid cartilage. Black silk sutures were used throughout.

The specimens were fixed in a solution of formaldehyde and Zenker's solution.

Dog 301.—A white male fox-terrier 6 or 7 years old underwent an operation for removal of the right lobe of the thyroid on Sept. 29, 1931. The dog remained healthy, with no apparent change in its habits or reactions. It was killed on June 1, 1932, at which time the left lobe of the thyroid was removed for comparison.

Dog 317.—A female beagle puppy about 10 months old underwent an operation for removal of the right lobe of the thyroid on Oct. 9, 1931. Recovery was uneventful, and the dog was in good health until October 24, when it contracted distemper. It died on Oct. 26, 1932. Autopsy revealed pneumonic consolidation of both lungs. The operative field was in good condition. The left lobe of the thyroid was removed for comparison.

Dog 320.—A female police dog about 2 years old underwent an operation for removal of the right lobe of the thyroid on Oct. 16, 1931. The left lobe was inspected. The dog remained well and healthy, with no change in its habits or reactions until it was killed on May 17, 1932, at which time the left lobe was removed. The operative field was in good condition. There was no apparent change in the size of the left lobe.

Dog 325.—A female fox-terrier about 2 years old underwent an operation for removal of the right lobe of the thyroid on Oct. 20, 1931. The left lobe was inspected. The dog remained healthy and in good condition with no change in its habits. It was killed on June 16, 1932, at which time the left lobe of the thyroid was removed. There was no apparent change in its size.

Dog 334.—A mongrel collie, a male, about 3 years old, underwent an operation for removal of the right lobe of the thyroid on Dec. 23, 1931, and the left lobe was inspected. The dog remained in good health with no change in its habits. It was killed in a fight on March 26, 1932. The left lobe of the thyroid was removed. There was no apparent change in its size.

Dog 303.—A brown female about 1 year old underwent an operation for removal of the right lobe of the thyroid and the left stellate ganglion on Sept. 30, 1931. Immediately following the operation the left pupil was contracted; both pupils reacted to light. Postoperatively the left pupil was contracted to one-half the size of the right pupil. Both reacted to light. Enophthalmos and lid lag were present in the left eye, and the conjunctiva was redundant over the sclera.

Three weeks postoperatively both eyes were the same, except for the pupillary difference. The right pupil was twice the size of the left. One month after the operation the dog had repeated convulsions. It was killed on October 30. Autopsy revealed pneumonia almost filling the entire right side. The operative site was in good condition. The left lobe of the thyroid was removed for study.

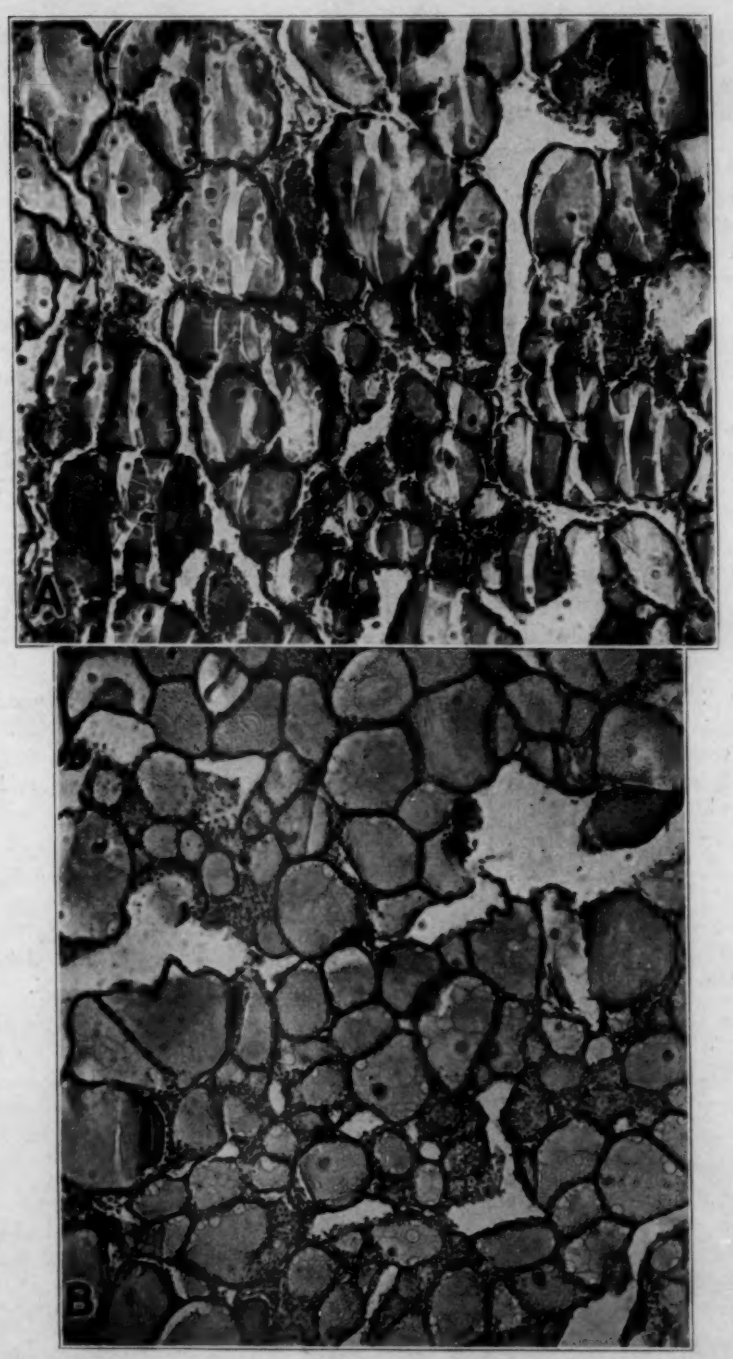

Fig. 1. (dog 320).—The effect of unilateral thyroidectomy on the remaining lobe. The photomicrographs show: *A*, a section of the right lobe, and *B*, a section of the left lobe taken seven months and one day after the removal of the right lobe. There are no striking differences.

Dog 305.—A black and tan female about 2 years old underwent an operation for removal of the right lobe of the thyroid and the left stellate ganglion on Oct. 5, 1931. Immediately following the operation the left pupil was one-half the size of the right pupil. Both pupils reacted to light. The dog remained in good health, with no apparent change in habits. During the next seven months of observation the left pupil was constantly smaller than the right; slight enophthalmos, lid lag and redundance of the conjunctiva persisted. Infection developed in a dog-bite wound in the thoracic wall on the left side, and the dog was killed on May 12, 1932. The left lobe of the thyroid was removed. There was no apparent difference in the size of the lobes.

Dog 318.—A large brown male from 4 to 5 years old underwent an operation for removal of the right lobe of the thyroid and the left stellate ganglion on Oct. 3, 1931. The usual changes were observed. The left pupil was one-half the size of the right. Both reacted to light. Enophthalmos, lid lag and redundance of the conjunctiva were present in the left eye. Lid lag and enophthalmos disappeared after four months. The animal remained healthy, with normal habits. It was killed on May 21, 1932. The left lobe of the thyroid was removed. There was no apparent change in size.

Dog 326.—A brown mongrel female about 8 months old underwent an operation for removal of the right lobe of the thyroid and the left stellate ganglion on Nov. 2, 1931. The usual changes occurred in the eyes. Four days after the operation the dog contracted distemper, and it died twenty-eight days postoperatively. The left lobe of the thyroid was removed.

Dog 336.—A mongrel male 1 year old underwent an operation for removal of the right lobe of the thyroid and the left stellate ganglion on Dec. 15, 1931. The usual changes occurred in the eyes. One month after the operation the dog contracted distemper, and it died on Jan. 30, 1932. The left lobe of the thyroid was removed.

Dog 358.—A black and white female about 1½ years old underwent an operation for removal of the right lobe of the thyroid and the left stellate ganglion on Feb. 15, 1932. The usual changes occurred in the eyes. The left pupil was one-half the size of the right. The conjunctiva was redundant. Enophthalmos and lid lag were not apparent. The dog remained healthy, with normal habits, until it was killed on June 6. The left lobe of the thyroid was removed.

Dog 304.—A brown and white male mongrel 2 or 3 years old underwent an operation for removal of the left stellate ganglion on Oct. 2, 1931. The usual changes occurred in the left eye: small pupil, enophthalmos, lid lag and redundant conjunctiva over the sclera. Enophthalmos and lid lag disappeared four months after the operation. The dog remained healthy, with normal habits. It was killed on May 25, 1932. The right and left lobes of the thyroid were removed.

Dog 307.—A black and tan female about 6 months old underwent an operation for removal of the left stellate ganglion on Oct. 6, 1931. The usual changes occurred in the eyes and persisted until death, although enophthalmos, lid lag and redundance of the conjunctiva gradually receded. The dog remained in good health and of normal habits. It was killed on June 8, 1932. The right and left lobes of the thyroid were removed.

Dog 321.—A brown female mongrel about 1 year old underwent an operation for removal of the left stellate ganglion on Oct. 20, 1931. The usual changes occurred in the left eye. The dog remained healthy, with normal habits. Corneal

ulceration and cataract developed in the left eye. It was killed on May 20, 1932. Both lobes of the thyroid were removed.

Dog 356.—A brown female about 1½ years old underwent an operation for removal of both stellate ganglions on Feb. 15, 1932. Both eyes showed immediate

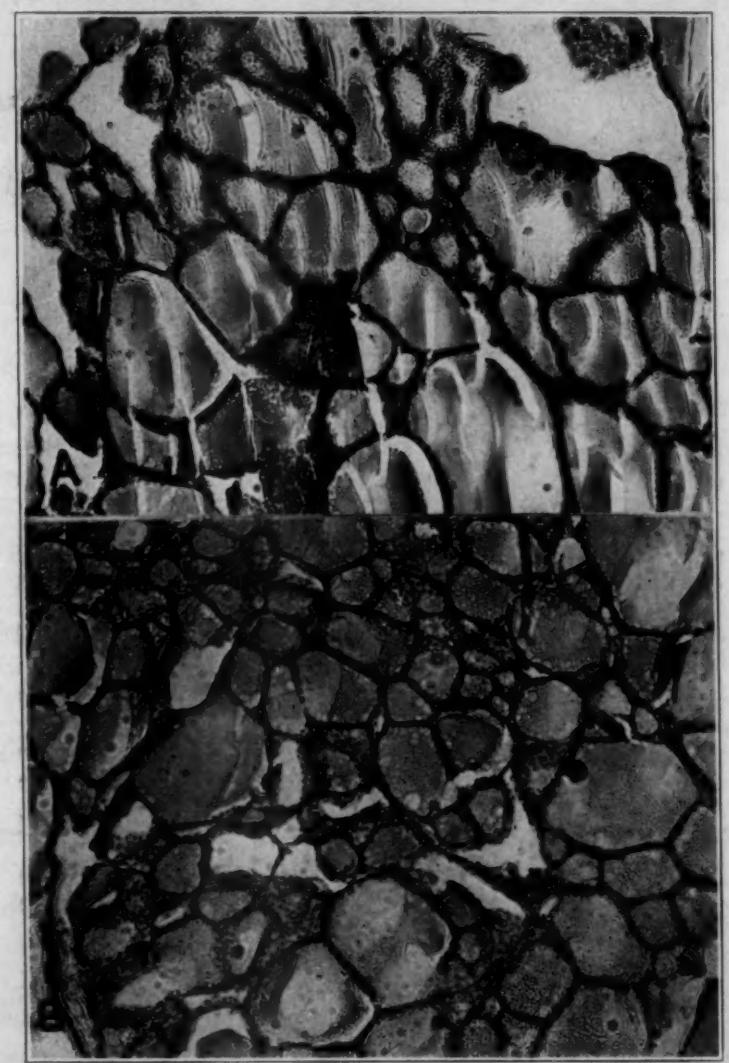

Fig. 2 (dog 307).—The effect of unilateral ganglionectomy on the thyroid gland. The photomicrographs show: *A*, a section of the left lobe, and *B*, a section of the right lobe. In spite of removal of the left stellate ganglion eight months and two days previously, there are no striking differences between the microscopic sections of the two lobes.

changes, i. e., contracted pupils, enophthalmos, redundant conjunctiva and slight lid lag. The enophthalmos and lid lag gradually decreased but persisted until death. The dog received 15 grains (0.975 Gm.) of thyroid extract three times a day at

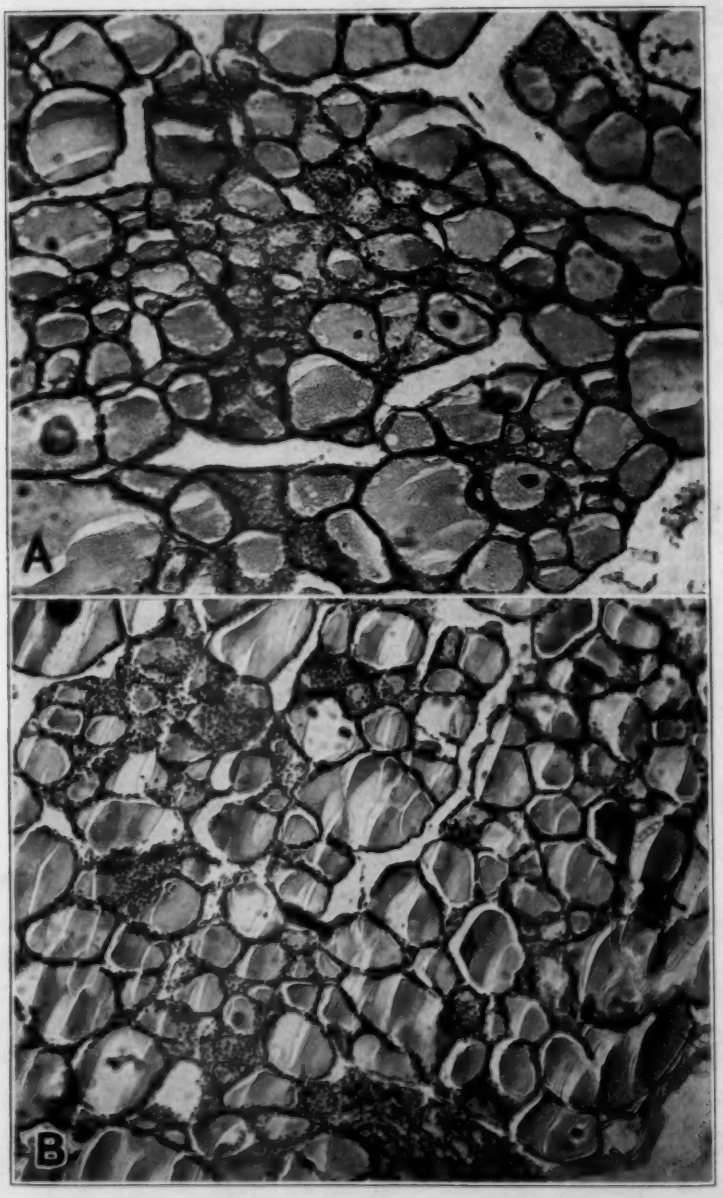

Fig. 3 (dog 326).—The effect of removal of the left stellate ganglion and the right lobe of the thyroid. The photomicrographs show: *A*, a section of the right lobe, and *B*, a section of the left lobe taken one month and one day after the operation. There is no appreciable difference between the microscopic sections.

various intervals, with coincident increase in the pulse rate and loss of appetite but no changes in the eyes. The dog was killed on June 2. The right and left lobes of the thyroid were removed.

PUPPY 1.—A small brown collie 6 weeks old underwent an operation for removal of the left stellate ganglion on Oct. 3, 1931. There were the usual changes on the left. The puppy progressed well for the first two weeks post-operatively and then rather suddenly went down-hill and died, probably of distemper, on October 29. At autopsy both lobes of the thyroid were removed. Intestinal worms were present.

PUPPY 2.—A small brown puppy 7 weeks old underwent removal of both stellate ganglions on Oct. 8, 1931. The eyes showed characteristic changes bilaterally. The puppy did well for three weeks and then gradually grew feeble and died. Autopsy revealed an abscess in the abdominal wall, probably secondary to an infected bite. The right and left lobes of the thyroid were removed.

OSTEOMYELITIS OF INFANTS

A DISEASE DIFFERENT FROM OSTEOMYELITIS OF OLDER CHILDREN

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Osteomyelitis of infants (children under 2 years of age), if one may judge from the literature, has usually been considered a rare disease not essentially different from the osteomyelitis of older children. This his been so contrary to our experience that we have reviewed the cases of patients of this age group treated at the Children's Hospital of Boston during the last twenty-one years—in all, 95 cases. In this survey we not only have considered the acute phases of the disease but have determined by recent clinical and roentgenographic examinations the present status of 41 patients treated in the orthopedic service during the aforementioned period. In some instances this observation was made as long as twenty years after the original infection.

We have included cases of both acute and chronic osteomyelitis in this study, although primary consideration has been given to the acute disease. On the basis of classifying a condition with a duration of one month or longer at the time of the patient's admission to the hospital as chronic, the condition in 82 of the 95 cases was acute and in 13 chronic osteomyelitis. In only 4 of the cases of so-called chronic osteomyelitis was the duration longer than three months; many cases were instances of healing acute osteomyelitis.

For general statistical information we have used the data on all the cases, but in the consideration of treatment we have used only those on cases of acute osteomyelitis, as it is only in those cases that the treatment was followed throughout the course of the disease.

In the entire series the mortality rate was 21 per cent. Separate consideration of the cases of infants under 6 months of age reveals a mortality rate definitely higher, 45 per cent, whereas in infants over 6 months and under 2 years of age the mortality rate was 14 per cent.

Read in part before the Boston Orthopedic Club, March 1933.

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AGE AND SEX

Osteomyelitis is reported as being most common between the ages of 8 and 16 years. For example, Wade,[1] of the Royal Alexandria Hospital for Children in Sydney, Australia, reported on 613 cases, in which the highest incidence was in children between 9 and 11 years. He stated that in his series there were few patients under 3 months of age and practically none between that age and 2 years.

On the basis of our experience, osteomyelitis in the younger group of children is not rare. This was particularly emphasized by the fact that in the Children's Hospital (age limit, 12 years) during the last two years there were more patients under 2 years of age than over 2 years, namely, 35. We do not believe that this represents a true relative age incidence, but it does suggest that osteomyelitis in this group is not unusual.

The patients in this series were evenly distributed through the various age groups under 2 years; 23 were under 6 months, the youngest being 11 days.

There were 50 boys and 45 girls. Osteomyelitis is more frequent in males than in females, and this has been ascribed to their greater exposure to trauma. On this basis one would not expect any particular difference in this series, and there was very little.

BONES INVOLVED

Klemm [2] reported that in 385 lesions the femur and tibia were almost equally involved, the femur in 111 instances and the tibia in 101. In our series 121 bones were involved in 95 cases: The femur was involved in 48 cases; the tibia in 18, the humerus in 16 and other bones less frequently. Multiple lesions were present in 12 cases, in 3 there being 4 or more. The femur was by all odds the bone most frequently involved.

The more rapidly growing end of the bone was involved in most cases. For example, in only 12 of the 48 cases of involvement of the femur was the lesion in the upper end; in 7 the neck was involved, and in 3, the greater trochanter. Likewise, in all of 9 cases in which the radius, with the preponderance of growth at the lower end, was involved, the lesion occurred in the lower end. In the tibia, where growth is little more rapid at the upper than at the lower end, the upper end was involved in 11 cases and the lower end in 7 cases.

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1. Wade, R. B.: Acute Osteomyelitis of Children, M. J. Australia **1**:264, 1929.

2. Klemm, P.: Beiträge zur Kenntnis der infektiösen Osteomyelitis, Beitr. z. klin. Chir. **84**:352, 1913.

PREDISPOSING FACTORS

Antecedent Infection.—The relationship of antecedent extra-osseous infection in this group is striking, in that 52 patients (table 1), or approximately 55 per cent, had undoubted preceding infections, as shown either by a definite history or by physical findings at the time of admission to the hospital. (We have not included such doubtful evidence as chronic tonsillitis and other questionable findings.) In 43 cases the evidence of infection either was doubtful or was omitted from the history. It is possible that in many instances the person recording the history neglected to inquire as to the presence of recent infection.

As may be seen in table 1, infection of the respiratory tract was present in 28 patients, or in approximately one half of the 52 in whom antecedent infection was known to be present. Of these, 20 had colds, bronchitis or sore throat, 3 had pneumonia with or without empyema, 2 had otitis media and 3 had infection of the respiratory tract with

TABLE 1.—*Relation of Extra-Osseous Infection and Trauma to Osteomyelitis*

	Cases		Cases
Incidence of antecedent infection	52	Incidence of trauma	16
Infection of respiratory tract	28	With antecedent infection	6
Cutaneous lesions	13	Without antecedent infection	10
Omphalitis	4		
Miscellaneous infections	7		
No known antecedent infections	43	No history of trauma	79

other abscesses. Antecedent infection of the respiratory tract occurred in 30 per cent of the total number of cases.

Antecedent cutaneous lesions were present in 13 cases, which was one fourth of those in which there was known to be an antecedent infection, or approximately 14 per cent of the entire group. The lesions were, specifically: furuncles, 4 cases; infected wounds, including burns, 4; impetigo, 2; paronychia, 1; scabies, 1, and eczema, 1.

Omphalitis was present in 4 cases, in each of which the patient was in the first weeks of life. Miscellaneous infections included: measles, 3 cases; chickenpox, 2; gonococcic septicemia (maternal origin), 1, and congenital syphilis, 1.

We should note that 5 patients had acute rickets and 2 were mongolian idiots, whose resistance to infection is notoriously poor.

Trauma.—The relationship of injury to osteomyelitis has been frequently debated. Ullmann, Lexer [3] and others [4] demonstrated that

3. Lexer, Erich: Zur experimentellen Erzeugung osteomyelitischer Herde, Arch. f. klin. Chir. **48**:181, 1894; Experimente über Osteomyelitis, ibid. **53**:266, 1896; Osteomyelitis: Experimente, ibid. **52**:576, 1896; General Surgery, translated by A. D. Bevan, New York, D. Appleton & Company, 1910.

4. Robertson, D. E.: Acute Hematogenous Osteomyelitis, J. Bone & Joint Surg. **25**:8, 1927.

osteomyelitis can be localized in experimental animals by injury to the bone after the injection of organisms into the blood stream. These experiments suggest that trauma may well be a factor in precipitating osteomyelitis in the presence of bacteremia or septicemia.

The clinical history of trauma is frequently unreliable, as pain in an extremity is often ascribed to vague injuries. Sixteen, or 17 per cent (table 1), of the patients had a history of local injury of minor degree; of these, 10 did not have a history of antecedent infection.

BACTERIOLOGY

The usual conception of osteomyelitis is that it is an infection due to Staphylococcus aureus. This conception is true of the condition in older children. Staph. aureus was the offending organism in 91 per cent of a series of cases in older children (from 2 to 12 years) observed in this hospital; however, in the group of infants, Streptococcus haemolyticus was by far the predominant organism.

Cultures were made in 76 of the 95 cases (table 2). This included not only cases in which a positive culture was obtained from material taken directly from the bone involved but also, in a few instances, cases in which there was definite clinical and roentgenographic evidence of osteomyelitis and a positive culture of the blood was obtained, although the bone itself was not exposed by operation. In 48 cases, or 63 per cent, there was a streptococcic infection; in nine tenths of these the organism was Str. haemolyticus. Staphylococcus was found to be present in 22 cases, or 30 per cent; of these, Staph. aureus was present in all except 2, in which Staphylococcus albus-haemolyticus was present. There were 3 cases in which Pneumococcus was present and 1 in which the gonococcus was identified by smear and by culture.

It is interesting to observe that in the cases with a history of antecedent infection of the respiratory tract the osteomyelitis was due to Streptoccocus in 22 of the 25 cases in which a culture was made, Pneumococcus was present in 2 cases and Staph. aureus in 2. In other words, the probability of the osteomyelitis being streptococcic, possibly pneumococcic, is certainly suggested in any case in an infant in which an antecedent infection of the respiratory tract was present.

Of the cases in which there were preceding cutaneous lesions, the organism was Staphylococcus in 8 and Streptococcus in 5; this is not a large preponderance of staphylococcic infection, but when one considers that in only 22 cases of the total group was Staphylococcus obtained, it increases the relative significance of the figure.

Organism Related to Mortality.—In the 48 cases in which a culture of Streptococcus was obtained there were 10 deaths, a mortality rate of 20 per cent (table 2). In the 22 cases in which a culture of Staphylo-

coccus was obtained there were 7 deaths, a mortality rate of 32 per cent. The higher rate in cases of staphylococcic infection is further emphasized when one considers only cases of acute osteomyelitis, in which the mortality rate from streptococcic infection was 19 per cent and that from staphylococcic infection was 41 per cent. Considering all cases in infants under 2 years, one sees that staphylococcic osteomyelitis definitely caused a higher mortality rate than streptococcic osteomyelitis.

In a separate consideration of the cases of infants under 6 months of age, one obtains a different picture. Of the 23 infants under 6 months of age, 10 had a streptococcic infection and 6 of these died, a mortality rate of 60 per cent; 5 had a staphylococcic infection and 2 of these died, a mortality rate of 40 per cent (table 2). This suggests that

TABLE 2.—*Bacteriologic Incidence, Showing a Relation of the Organism and Age to Mortality*

	All Patients			Patients Under 6 Mo. of Age			Patients from 6 Mo. to 2 Yr. of Age		
Organism	Patients	Deaths	Mortality, per Cent	Patients	Deaths	Mortality, per Cent	Patients	Deaths	Mortality, per Cent
Streptococcus	48	10	20	10	6	60	38	4	10
Staphylococcus	22	7	32	5	2	40	17	5	30
Pneumococcus	3	1	..	0	0	..	3	1	..
Gonococcus	1	0	..	0	0	..	2	0	..
Undifferentiated coccus	2	0	..	1	0	..	0	0	..
Cases in which culture was recorded	76	..	..	..	..	..	..	..	..
Cases in which culture was not recorded	19	2	..	6	2	..	13	0	..
Total	95	20	21	22	10	45	73	10	14

streptococcic osteomyelitis is relatively more virulent in infants under 6 months of age than in older infants.

Chronic Osteomyelitis.—Of the 13 cases of chronic osteomyelitis, there were 8 in which a culture was made. In 5 Staph. aureus was present; in 2, Strep. haemolyticus, and in 1, Pneumococcus.

When one considers the relative infrequency with which Staphylococcus is isolated in cases of acute osteomyelitis of infants (25 per cent), the presence of this organism in 5 of the 8 cases of chronic osteomyelitis would seem to have some significance, although there are too few cases for one to draw any conclusions. Staph. aureus seems to produce chronic osteomyelitis more frequently than Str. haemolyticus, even in infants.

Blood Culture.—Cultures of the blood were not made as a routine procedure and usually were made only when the patient was severely ill. Of the cultures of the blood recorded for 24 cases, 10 yielded Streptococcus, 6 Staph. aureus and 1 Staph. albus-haemolyticus, and 7

gave negative results. Six of the ten patients with streptococcic septicemia died, and 4 of the 6 with staphylococcic septicemia died.

Comment.—The outstanding frequency of streptococcic infection in cases of osteomyelitis in young children is possibly due to a greater general susceptibility to such infection in infants and is, in part, an indication of the types of infection which they contract. For example, sepsis of the joints of infants is likely to be streptococcic, increasing numbers of cases of staphylococcic infection being observed in the later years. This suggests that the infant has relatively less natural immunity to certain strains of Streptococcus than to Staphylococcus and that from repeated infection an acquired immunity develops to Streptococcus, which becomes more effective as the infant grows older; this is not so outstanding with Staphylococcus. This suggestion is enhanced by the fact that the mortality rate from streptococcic osteomyelitis is much higher in infants under 6 months of age than in older children.

SYMPTOMATOLOGY AND DIAGNOSIS

The early clinical picture of acute osteomyelitis in infants is not essentially different from that seen in older children, namely acute illness, with the general systemic manifestations provoked by sepsis together with local pain and sensitivity of the involved part (see the reports of cases). The severity of the onset and subsequent illness is as variable in this group as in older children. To illustrate this variability we have classified the cases in this series according to the severity of the condition at the time of admission to the hospital into four divisions: (1) those in which the patient was not severely ill, 15; (2) those in which the patient was severely ill but not critically so, 26; (3) those in which the patient was critically ill, 20, and (4) those in which the patient was moribund and the prognosis was considered totally bad, 13. To clarify this classification further, we should comment that in group 1 some of the patients had a temperature as high as 102 F. and a white blood cell count as high as 20,000 per cubic millimeter of blood.

Of the local findings, protection and muscle spasm were recognized earliest. Tenderness at the metaphysis is not a reliable sign at this age, though usually with patience definite information may be obtained. Local edema comes on more rapidly in infants than in older persons and is much more diffuse; in fact, the entire extremity may be swollen from a process involving a single bone, even though the infection has not perforated the periosteum. Although ordinarily the swelling is maximal at the site of the lesion, frequently it is not circumscribed enough to define the area involved.

Differential Diagnosis.—The differential diagnosis may be difficult before changes occur in the bone which are visible in roentgenograms. The more common confusing possibilities are sepsis of the joint and

infection of the soft tissue; scurvy, with infection elsewhere, and syphilis are less confusing. Rheumatic fever is not a consideration at this age.

Sepsis of a joint frequently causes diffuse swelling surrounding the joint, though usually the swelling is not as widespread as in cases of osteomyelitis. The presence of a resistant flexion deformity, marked muscle spasm and pain on motion, associated with synovial tenderness and distention of the capsule, suggests sepsis of the joint. Occasionally a joint may show considerable distention with fluid provoked by adjacent osteomyelitis without the joint's being infected, but the amount of fluid in a joint so involved is less than one would expect from the severity and duration of the infection, and motion is less painful. Aspiration of the joint through clean tissue may be necessary before the diagnosis can be made, and even then it may be necessary to await culture of the fluid. Sepsis of a joint secondary to adjacent osteomyelitis is always a possibility, as in infants secondary sepsis of the joints is more common than in older patients.

Ordinarily superficial cellulitis is easily differentiated, but cellulitis or abscess of the deeper fascial layer and suppurative bursitis may be very perplexing, and often preoperative differentiation cannot be made. If involvement of the part is most marked at a distance from the epiphysis, it is suggestive of a process in the soft tissues. Osteomyelitis in children almost uniformly has its origin adjacent to the epiphysis.

The multiplicity of the lesions, the general picture and the laboratory observations serve to differentiate syphilis. As far as scurvy is concerned, the prime consideration is to keep it in mind in arriving at the diagnosis.

Roentgenography.—Roentgen examination is of more diagnostic aid for infants than for older children or adults, since the lesions are visible at a somewhat earlier period in the disease. The distribution of edema in the soft tissue as visible in the roentgenograms is occasionally helpful. Likewise, the roentgenograms may be of aid in the differential diagnosis by demonstrating the distended capsule of a septic joint or by suggesting the presence of scurvy or syphilis.

In addition to early juxta-epiphyseal rarefaction, one should look for the formation of subperiosteal new bone, which occasionally is the first abnormality that can be observed.

Roentgenographic observations of the course of the disease are illuminating. The subperiosteal new bone (involucrum) is visible much sooner than in older persons; it usually involves half the length of the bone and frequently suggests that sequestration of the shaft will occur, but, as will be seen later, this rarely happens. The healing process as visible in the roentgenograms likewise occurs much more rapidly than in older persons.

PROGNOSIS

Immediate Prognosis.—Of the 82 patients with acute osteomyelitis, 18 died—a mortality rate of 22 per cent. Seventy-one of the 82 patients were operated on, 11 were not. Of the latter group, 3 patients were moribund when they were admitted to the hospital and died almost immediately. Fifteen deaths occurred in the cases in which operation was performed (table 3).

Period of Hospitalization.—The average period of hospitalization of the patients who recovered was six weeks. In this connection we should point out that frequently the patient was kept in the hospital until the sinus had closed or at least needed no further packing. In only 6 instances was the patient admitted more than once, and in 3 this was for the care of secondary lesions of joints.

TABLE 3.—*Immediate Prognosis*

	Number of Patients	Deaths	Mortality, per Cent
Acute osteomyelitis	82	18	22
Chronic osteomyelitis	13	2	15
Total	95	20	21
Average period of hospitalization			6 weeks
Average duration of sinus			12 weeks
Recurrences			2 cases
Sequestration			6 cases

Duration of the Sinus and Recurrences.—The average time from the onset until the sinus had healed was twelve weeks, although by omitting 3 cases this average could be reduced to eight and one-half weeks. In all but 3 of the 56 cases of acute osteomyelitis in which operation was performed, healing was complete in four months; in 31 of the 56 healing was complete at the end of two months.

Once the sinus was healed, in only 2 cases was there a recurrence. In both instances drainage persisted for two weeks, and the sinus closed voluntarily and remained healed.

Sequestration.—Sequestration was comparatively rare. In only 6 cases was sequestrectomy necessary; these were the only cases in which gross sequestrums were present, although in 2 cases of osteomyelitis of the neck of the femur there was a gradual absorption of the head after the sinus was healed. As previously mentioned, roentgenograms made during the course of the disease frequently suggested that sequestration would occur, but it did not materialize.

In only 20 of the 95 cases was there more than one operation, and in 10 of these the operation was for a lesion other than the primary osteomyelitis.

In considering the foregoing factors alone, one conceives that the course of osteomyelitis in infants is quite different from that in older children. In infants there is a pleasing contrast from the frequently prolonged disease with long periods of hospitalization and repeated surgical procedures that are commonly observed in older children.

Complications.—The most common complications were lesions of other bones, sepsis of joints, pneumonia and abscesses, both fascial and visceral. Twelve patients had lesions of more than one bone. Sepsis of joints occurred in 11, in 9 by apparent extension from an adjacent bone, and in 2 as a metastatic lesion without evident involvement of adjacent bone. Of the first mentioned group, 4 had involvement of the hip joint from adjacent osteomyelitis of the neck of the femur, 3 involvement of the knee joint from the femur and 2 involvement of

TABLE 4.—*Survey of End-Results in Fifty-Four Cases in the Orthopedic Department*

Total Patients	Living	Deaths	Follow-up Examination in 1933	No Follow-up Examination; Well Last Visit
54	46	8	41	5
Present status of lesion in 41 patients				
Entirely healed clinically and by roentgen examination				39
Healing incomplete; recent case; under treatment				1
Clinically well but roentgenograms suggest residual infection				1
Residual deformities				
Deformity present; in 4 from secondary lesions of joints				5
None				36

the ankle, in 1 from tibia and in 1 from the fibula. There was also 1 with involvement of the elbow joint from the lower end of the humerus.

Of the 20 patients who died, postmortem examination was carried out on 10. With one exception, all the patients in this group had demonstrable septicemia. Eight had multiple abscesses; the organs usually involved were the liver, heart, kidneys, lungs and skin. All but 1 had bronchopneumonia; this was particularly extensive in the 2 patients who did not have multiple abscesses. However, bronchopneumonia is observed rather commonly at postmortem examination, and in 1 case the pneumonia was considered terminal. Two of the patients with multiple abscesses had vegetative endocarditis.

Final Prognosis.—The most interesting side of this study has been a recent follow-up examination of 54 patients treated in the orthopedic service. The present status of 41 of the 46 who recovered was recently determined by physical and roentgen examination (table 4). Many of those examined had had osteomyelitis from ten to twenty years previously.

Only 2 patients in the entire group showed evidence of the persistence of osteomyelitis. The case of 1 child, aged 2 years, in whom

in November 1932 there developed acute osteomyelitis of the neck of the femur, the ilium and the fibula associated with staphylococcic septicemia, is subsequently discussed as case 7. The other patient had acute osteomyelitis of the femur in 1927, and although she has been free from symptoms since that time, with unlimited activity, roentgenograms suggest the presence of a smoldering lesion. In 2 cases a recent examination showed considerable residual thickening of the bone but no clinical or roentgenologic evidence of activity (case 2). Roentgenograms in the other cases showed the lesions to be healed.

There were 5 cases with resultant deformity. In 4 the defect resulted from secondary sepsis of the joint; in the other, after a too extensive operation very early in the course of the disease, the radius regenerated poorly, with ankylosis to the ulna. Of the cases of deformity due to involvement of the joints, in 2 the deformity was of the hip, with absorption of the head of the femur, in 1 of the knee, with ankylosis, and in the other of the elbow. The last-mentioned case was one of recent involvement; there was little residual deformity, and the condition is still improving.

There was some tendency for the involved bone to be a little shorter than its fellow in 5 cases, but in no instance except when the joint was involved was the difference over ½ inch (1.2 cm.). There were no cases of residual lengthening.

The present status of the younger patients forms a striking contrast to the usual picture of osteomyelitis. We have been able to determine the present state of 41 of the 46 patients now living who were treated in the orthopedic service; in only 2 cases was there any suggestion of the presence of residual osteomyelitis, 1 a recent case in which there was healing and another a case in which there were no symptoms. In all but 1 case the deformity was due to involvement of the joint. In many cases of extensive destruction during the acute process one could find evidence of the original lesion in the roentgenograms with difficulty, and in several, not at all.

This contrast to the picture of the disease in older children is further emphasized by the relatively brief duration of the disease in infants, with rapid healing, infrequent sequestration and rare recurrences.

TREATMENT

For consideration of the treatment of acute osteomyelitis we have classified the cases in two groups: 71 cases in which there was surgical intervention and 11 cases in which treatment was nonoperative. The first group may be subdivided as follows:

1. Thirty-seven cases in which drainage of the bone was done by a surgical procedure directly on the bone. In the majority of these a

window was made through the cortical bone, though in a small percentage drill holes were made for drainage.

2. Thirty-four cases in which indirect drainage of the bone was done without surgical attack on the bone itself. In the majority of these the periosteum had ruptured at the time of operation and simple surgical drainage of the secondary abscess was performed. In 8 cases the periosteum was incised before it had ruptured, and in all but 2 pus was obtained.

In the other group, 11 cases, nonoperative treatment was carried out by election on 8 patients, and the other 3 were moribund on admission and died soon thereafter.

Surgical Treatment.—Direct Surgical Attack on the Bone: In general the treatment in the cases in which a direct decompression of the marrow spaces was carried out through a window of moderate size in the bone represents the usual conception of the ideal treatment of osteomyelitis. There might be criticism because of the interval of time that was allowed to elapse from the onset of the disease to the operation in many instances. In general, it is somewhat longer for this group than for older children, for whom the diagnosis can be made more easily and examination is made earlier in the course of the disease. However, in answer to this criticism, those operated on after a relatively long interval did as well as those operated on very early, as regards both the immediate and the final result; in fact, the 2 patients having the longest and stormiest postoperative convalescence underwent a surgical procedure on the first and second day, respectively, after the onset.

Case 1 is representative of the cases in which drainage was accomplished by a window in the bone.

CASE 1.—*Osteomyelitis in the lower end of the right femur.*

G. C., a girl aged 1 year, was admitted to the hospital on April 7, 1932, with a complaint of irritability and pain in the right lower extremity of four days' duration. Her health previously had been good. There was no history of immediate antecedent infection or injury.

Examination disclosed a moderately ill child, with a diffuse swelling of the lower third of the thigh, with tenderness maximal at the lower end of the femur. A relatively normal range of painless motion was possible at the knee joint. The roentgenograms of the femur were normal except for edema of the soft tissues. The temperature was 103.4 F. The white blood cell count was 27,000 per cubic millimeter.

At operation a window was made in the lower end of the femur. The wound was packed open with gauze impregnated with petrolatum, and the extremity was immobilized in a plaster hip spica. The organism present was Str. haemolyticus.

A roentgenogram made postoperatively, on May 5, showed mottled rarefaction of the lower third of the femur, with periosteal reaction about the lower half of the shaft.

The patient was discharged from the hospital on June 3. The sinus healed two and one-half months after the onset.

Final examination in October 1933 (eighteen months after the onset) showed the extremity to be normal in all respects except for the postoperative scar. Roentgenograms at this time showed little evidence of the former lesion (fig. 1).

The child was moderately but not critically ill. She was operated on the day after she was admitted to the hospital, which was five days after the onset. There was no pus immediately beneath the periosteum,

Fig. 1 (case 1).—*A*, made one month after the onset, shows mottled destruction of the lower third of the femur, with subperiosteal new bone about the lower half of the shaft. *B*, made one and one-half years later, shows little evidence of the former lesion. Treatment was by surgical intervention; a window was placed in the bone adjacent to the epiphysis.

but a moderate-sized window in the cortex revealed pus. The wound was packed open with petrolatum gauze, and the part was immobilized in a hip spica which was bivalved. Dressings with replacement of the petrolatum gauze were done at weekly intervals. There was uneventful and rapid recovery, and although the early roentgenograms showed

mottling of the lower third of the femur, with considerable subperiosteal new bone (involucrum), there was no gross sequestration.

Although this was the usual picture, not all in this group had such an uneventful course, and in 2 cases there was extensive sequestration of the type seen in older persons. Case 2 is an example.

CASE 2.—*Osteomyelitis of the upper shaft of the left femur.*

J. M., a boy aged 1 year and 1 month, was admitted to the hospital on Dec. 27, 1927, with a complaint of acute illness for four days and pain in the left thigh for twenty-four hours. There was a history of a boil one month before the onset and of a fall on the day of the onset without apparent injury.

Examination disclosed a severely ill child, with slight swelling of the upper one third of the thigh and marked tenderness, maximal over the upper end of the femur. Gentle motions of the hip joint were not particularly limited. The temperature was 104 F. The white blood cell count was 22,000 per cubic millimeter. A blood culture showed Staph. aureus. Roentgenograms gave negative results.

At operation on the day of admission a window was placed in the upper portion of the femur below the greater trochanter. Pus was present beneath the cortex. The wound was packed open with petrolatum gauze. Immobilization was accomplished in a plaster spica. The organism isolated from the wound was Staph. aureus.

Roentgenograms made postoperatively on Jan. 30, 1928, showed extensive rarefaction of the proximal half of the shaft of the femur, with a large involucrum surrounding the bone throughout its length. On May 11 roentgen examination revealed the involucrum to be even more extensive, with definite sequestration of a large part of the shaft. The wound continued to drain.

Sequestrectomy was carried out in June 1929. The sinus closed in April 1930, two years and four months after the onset.

Final examination on Feb. 3, 1933, five years and two months after the onset, revealed the child to be entirely well. Roentgenograms made at this time showed marked thickening of the shaft, but there was no other evidence of residual infection (fig. 2).

This child was likewise operated on on the day of admission, which was possibly four days after the onset, although there had been symptoms referable to the local area for only twenty-four hours. The window was farther from the greater trochanter than the ideal site, but pus was obtained, the wound was packed open and the part was temporarily fixed in plaster, although afterward the extremity was only intermittently immobilized, and dressings were changed frequently.

The large sequestrum, the slowly healing sinus and the residual thickening suggest the usual picture of osteomyelitis in older persons rather than that seen in infants. It was most unusual in this series. In the only other patient who showed an extensive sequestrum, a window was made on the second day after the onset, and the organism was likewise Staph. aureus. One might suspect that the formation of a sequestrum was typical of staphylococcic osteomyelitis, even at this age, except that in only 3 of the 22 cases in which this organism was present was a sequestrectomy necessary. By comparison, in only 3 of the 48 cases of streptococcic osteomyelitis was a sequestrectomy needed, and

there were no sequestrums of the size seen in the 2 cases reported. Staphylococcic osteomyelitis, even at this age, seems more likely to produce extensive sequestration than streptococcic osteomyelitis.

Drainage Without Surgical Attack on the Bone: The 34 cases in this group represent a less orthodox method of therapy, though, as mentioned by Lewis,[5] simple incision for patients of all ages was advocated

Fig. 2 (case 2).—*A* shows a picture of osteomyelitis as frequently seen in older children. Only in this case and in one other was this type of sequestration observed. The roentgenogram made just previous to sequestrectomy shows the sequestrum well outlined. *B*, made three and one-half years later, shows residual scarring but no evidence of activity. There have been no symptoms for two years. The primary surgical procedure was the formation of a window in the bone four days after the onset.

by Trendelenburg, Wilms and Sauerbruch. At the time of operation the bone was not disturbed; in the majority of cases the procedure

5. Lewis, Dean: Acute Osteomyelitis, J. A. M. A. **92**:783 (March 9) 1929.

consisted merely of making an incision into the secondary abscess, packing it wide open with petrolatum gauze and immobilizing the part. The following cases may be considered in this group.

CASE 3.—*Osteomyelitis of the right ulna.*

R. L., a boy aged 1 year and 8 months, was admitted to the hospital on July 16, 1932, with a complaint of acute illness and pain in the right upper extremity of five days' duration. His health previously had been good, but he had had a rather severe infection of the respiratory tract for the two weeks preceding the present illness. The arm had been immobilized for four days immediately preceding admission.

Examination revealed the child to be moderately ill, with a marked, diffuse, tender swelling from the wrist extending upward beyond the elbow. Motions of the elbow and wrist joints were normal. The temperature was 103.6 F. The white blood cell count was 23,000 per cubic millimeter. Roentgenograms gave negative results, except for evidence of swelling of the soft tissues.

At operation the abscess was drained (the bone was not explored). Immobilization was effected. A culture of material from the wound showed Str. haemolyticus.

On August 16 the roentgenologists reported considerable destruction of the ulna with a large amount of irregular bone surrounding it. The shaft seemed to be forming a sequestrum.

The wound healed in six weeks.

Final examination on Feb. 27, 1934, eighteen months after the onset, revealed the lesion to be entirely healed. The roentgenogram at this time showed the bone to be apparently normal (fig. 3). The sequestrum did not materialize.

CASE 4.—*Osteomyelitis of the lower end of the left radius.*

E. L., a girl aged 1 year, was admitted to the hospital on Nov. 20, 1932, with a complaint of an acute illness of twenty-four hours' duration, associated with pain and swelling of the left forearm. The child's general health had been good previous to the present illness except for an infection of the respiratory tract during the preceding week.

Examination revealed the child to be quite ill, with tender swelling of the distal half of the left forearm. Movement of the wrist joint was not particularly painful. The temperature was 104.2 F. The white blood cell count was 29,400 per cubic millimeter. A roentgenogram showed no abnormalities.

At operation on November 21, the abscess was drained, the wound was packed with petrolatum gauze and the arm was immobilized in plaster. A culture of material from the wound showed Str. haemolyticus.

On December 23 the roentgenologists reported that the radius showed a considerable amount of generalized mottled absorption of practically the entire shaft, with a moderate amount of subperiosteal new bone surrounding the shaft.

The sinus healed two months after the onset. In February 1934, fifteen months after the onset, the forearm was apparently normal on both clinical and roentgen examination (fig. 4).

CASE 5.—*Osteomyelitis of the upper end of the left tibia.*

H. F., a boy aged 4 months, was admitted to the hospital on Dec. 28, 1932, with a complaint of an acute illness of five days' duration, associated with pain in the left leg. The day before admission to the hospital the patient would not move his leg, and the mother noted that it was swollen. His health, previous to a per-

Fig. 3 (case 3).—*A*, made one month after the onset, shows extensive destruction throughout the shaft of the ulna, with an irregular depositon of new bone. *B*, made two months later, shows healing, and *C*, made eighteen months later, shows the ulna apparently normal. Treatment was limited to drainage of the abscess.

Fig. 4 (case 4).—*A* shows extensive destruction throughout the shaft of the radius and *B*, the bone apparently normal fifteen months later. Treatment was limited to drainage of the abscess.

sistent infection of the respiratory tract which had developed one month before, had been good.

Examination revealed the child to be critically ill, with a diffuse, tender swelling of the leg, maximal just below the knee. The temperature was 106.2 F. The white blood count was 30,000 per cubic millimeter. A roentgenogram showed nothing abnormal.

At operation the abscess was drained, the wound was packed with petrolatum gauze and the leg was immobilized in a plaster cast. Culture from the wound showed Str. haemolyticus.

A roentgenogram made on Jan. 10, 1933, showed irregular destruction throughout the shaft of the tibia, with a surrounding involucrum extending the length of the bone. There was slight anterior and lateral displacement of the upper epiphysis of the tibia.

Fig. 5 (case 5).—*A*, made three weeks after the onset, shows marked destruction of the shaft of the tibia, with displacement of the upper epiphysis. *B*, made one month later, shows remarkable healing in a brief period. Note the suggested narrowing of the epiphyseal line. Treatment was limited to drainage of the abscess.

The wound healed in three months.

Roentgenograms made on February 20, three months after the onset, showed healing, with no evidence of sequestration. There was a suggestion of narrowing of the epiphyseal line (fig. 5).

In all 3 of the patients localization had occurred, and the pus had ruptured through the periosteum. The surgical procedure consisted merely of draining the abscess in the soft tissue adequately and of immobilizing the part. All the patients were severely ill at the time of admission, and the roentgenograms made subsequently in each case

suggested extensive sequestration, although in no instance did this occur The sinuses healed rapidly, as did the bone.

These cases are representative of the group in which drainage was accomplished without attacking the bone, although also in this group are those cases in which the periosteum was incised either before or after the presence of gross pus. Case 5 is reported because the early roentgenogram showed displacement of the epiphysis (the child's extremity was not protected for the five days previous to admission), and the final one suggested some residual narrowing of the epiphyseal line.

A statistical comparison of those cases in which treatment by drainage of the abscesses of the soft tissue was employed and those in which direct drainage of the bone was used has shown little difference in either immediate and final outcome. In the amount of bone involved, as viewed by subsequent roentgenograms, metastatic lesions and the interval for the sinus to heal, no differences were noted. Of the 37 patients treated by operation on the bone, 7 died; of the 34 treated by drainage of abscesses of the soft tissues, 8 died. However, it is difficult to make a direct statistical comparison unless contrasting operations are carried out on patients with a similar condition, and only more recently has this been done. For example, in some of the cases in which drainage of the abscess alone was carried out, the patient was in such poor condition that no more could be done. This was naturally unfavorable to the statistics for the group.

It is interesting that there was only 1 case in the group in which simple drainage was used in which it was necessary to perform a sequestrectomy. In this case operation was performed on the second day of the disease, and the periosteum was incised before localization had occurred; subsequently it was necessary to remove a sequestrum the size of a pea. On the other hand, in case 5, with similar treatment, there is some residual narrowing of the epiphyseal line, and it will be necessary to follow this case to see whether or not growth is in any way affected.

Nonsurgical Treatment.—Of the 8 patients who by choice were treated without surgical intervention, 2 were critically ill, with cultures of the blood showing, respectively, Str. haemolyticus and Staph. aureus; 1 was moderately ill, and 5 were mildly ill. The following case is representative of those of the mildly ill patients.

CASE 6.—*Osteomyelitis of the neck of the right femur.*

M. M., a girl aged 1 year, was admitted to the hospital on Nov. 21, 1931. Ten days previously the child became irritable and feverish and refused to walk. She was not particularly ill, but all motions of the hip were painful. There was only moderate muscle spasm. The temperature was 100.6 F. The white blood cell

count was 22,000 per cubic millimeter. The reaction to tuberculin was negative. Roentgenograms showed an area of absorption in the neck of the femur.

Nonsurgical treatment was instituted, with immobilization by means of a wire splint with the leg in abduction. Roentgenograms made on Jan. 19, 1932, showed rarefaction of the neck of the femur, with a subperiosteal deposit of new bone about the upper third of the shaft of the femur.

Final physical examination on Feb. 24, 1933, fifteen months after the onset, showed the extremity to be normal. Roentgenograms made at this time showed complete healing, with slight residual thickening of the neck. The organism was not known (fig. 6).

The 5 mildly ill patients who were treated by immobilization recovered completely as did the patient in case 6. The following case is one in which a critically ill patient was treated without surgical intervention.

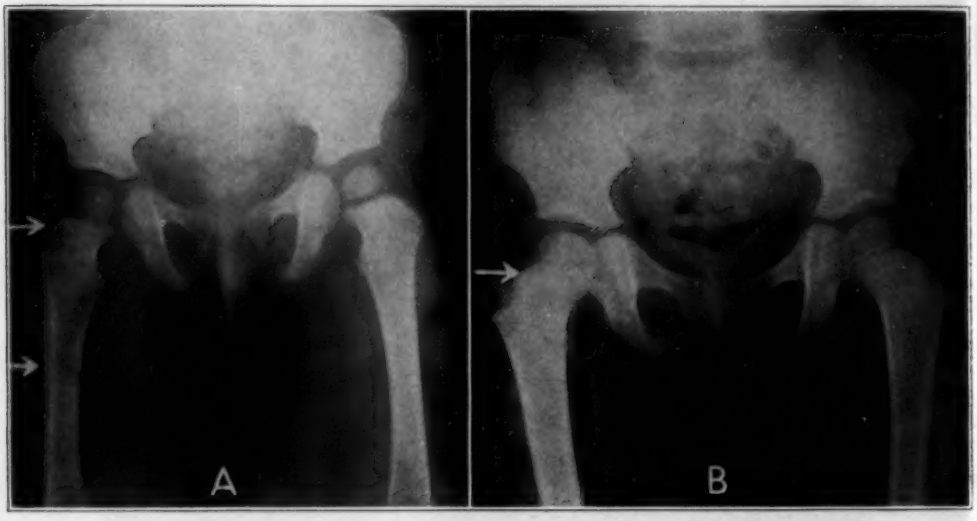

Fig. 6 (case 6).—*A* shows an area of destruction in the neck of the femur, with mild subperiosteal reaction for half the length of the shaft. *B*, made thirteen months later, shows the lesion completely healed. Treatment was by immobilization, without surgical intervention.

CASE 7.—*Osteomyelitis of the neck of the left femur.*

A. M., a boy aged 2 years, was admitted to the hospital on Nov. 4, 1932, with a complaint that three days before pain had developed in the left lower extremity, associated with a rapidly developing acute illness. The past history was significant in that the patient had recently had several boils, and two days before the onset of the present illness he had fallen on a furuncle of the right buttock, rupturing it.

Examination revealed a critically ill, rather stuporous child, with his left hip held in flexion by muscle spasm. There was a suggestion of fulness over the capsule of the hip joint. Tenderness could not be definitely localized. When the extremity was handled with care a large amount of relatively painless motion at the hip joint could be obtained and the flexion deformity could be reduced. The

temperature was 106 F.; the pulse rate was 180, and the white blood cell count was 23,000 per cubic millimeter. Repeated cultures of the blood yielded Staph. aureus.

At the time of admission the diagnosis was not definitely made, though osteomyelitis of the neck of the femur was suspected.

Nonsurgical treatment was instituted, with immobilization by traction and general systemic support. The temperature progressively approached normal. Improvement was so marked that by the time the diagnosis could be made definitely, continued conservative therapy was indicated.

A roentgenogram made on November 14, ten days after admission, showed a slight amount of irregular erosion of the neck of the femur adjacent to the epiphyseal line. Lesions were demonstrated in the left fibula as well as in the right ilium.

The temperature was normal from the fourteenth day after admission, except on one occasion, when following removal of traction there was immediately a flare-up of fever, with subsidence when the traction was replaced.

A roentgenogram made on Jan. 23, 1933, the first which included the lower end of the right femur, showed an area of rarefaction adjacent to the distal epiphysis; the other lesions were smaller and less distinct. A roentgenogram made on February 15, fourteen weeks after the onset, showed further healing, and at that time the patient was given a non-weight-bearing brace and was discharged from the hospital.

Following overactivity at home he returned on March 23, with a temperature of 103 F. and marked muscle spasm, with limitation of all motions of the hip. The white blood cell count was 15,600. A culture of the blood gave negative results. Traction was applied to the extremity. The muscle spasm rapidly disappeared, and there was subsidence of the temperature to normal by the fifth day after admission. The patient was discharged in a hip spica on April 20, one month after admission.

The last roentgenogram made, in August 1934, showed the lesion of the femur to have decreased in size, but it was not healed completely. All motions of the hip were painless. The area in the ilium was still visible in the roentgenogram, although at no time had the patient had symptoms referable to this area (fig. 7).

The following case, in which osteomyelitis of the neck of the femur was treated by surgical intervention, is reported for contrast with case 7.

CASE 8.—*Osteomyelitis of the neck of the right femur.*

H. P., a boy aged 1 year and 2 months, was admitted to the hospital on Dec. 9, 1929. The onset, on November 14, was marked with a temperature of 103 F. and pain in the right thigh. The symptoms continued until the time of admission. The child was not particularly ill but protected his right hip, which showed a deformity of 45 degree flexion, with all motions painful and a suggestion of distention of the capsule of the hip joint. The temperature was 100.2 F. The white blood cell count was 17,000 per cubic millimeter. A roentgenogram showed an area of rarefaction adjacent to the epiphyseal line.

Operation was performed on December 12. A window was made in the neck of the femur by posterior incision (according to the method of Ober). There was no pus in the joint, but thick purulent material was present in the neck of the femur. A drain of rubber dam was introduced. The organism present was Staph. aureus. Traction was used, though not constantly, until Jan. 23, 1930, when a plaster spica was applied and the child was discharged from the hospital.

A roentgenogram made on January 20 showed destruction of the greater part of the head of the femur, with lateral luxation.

On final examination, on March 4, 1933, the child walked with a lurch on the right, with the extremity in about 25 degrees of external rotation. Although the hip was fairly stable, there was limitation of all motions, with extension to neutral, flexion to 55 degrees and external rotation to within 15 degrees of neutral.

Fig. 7 (case 7).—*A*, made one month after the onset, shows extensive destruction in the neck of the left femur, with a reaction in the upper third of the shaft. There is an area of rarefaction in the ilium also. *B*, made three months later, shows considerable healing; the arrows indicate areas of destruction. *C*, made nine months later, shows the lesion in the lower end of the femur nearly healed. The upper lesion has not yet healed and is still under treatment. Treatment was by immobilization, without surgical intervention.

There was 5/8 inch (1.5 cm.) shortening. A roentgenogram showed absence of the head, with the neck articulating with the acetabulum (fig. 8).

Case 8 is an example of those cases of osteomyelitis of the neck of the femur in which treatment was surgical. Of the 3 cases, there were slow disintegration and complete destruction of the head of the femur in 2, and in the third the patient died.

On the other hand, of the 3 patients with osteomyelitis of the neck of the femur treated without operation, 2 were well at the time of the last examination, whereas the third (case 7), although desperately ill on admission, with an extensive process, multiple lesions and Staph. aureus septicemia showed healing, though roentgenograms showed that the lesion was not completely healed. Even if the drainage of the small residuum is necessary later, it should not disturb the circulation of the head of the femur. This patient's lesions healed slowly, but it is to

Fig. 8 (case 8).—*A*, made three weeks after the onset and just previous to operation, shows the large area of destruction in the neck of the right femur. *B*, made three years later, shows complete destruction of the head of the femur. Treatment was by surgical intervention, a window being made in the bone.

be remembered that the child was at the upper limit of the age group, 2 years, and that the organism was Staph. aureus.

A younger child, with osteomyelitis of the neck of the femur and the blood showing Str. haemolyticus, almost as sick as the patient in case 7, was treated without surgical intervention. The patient is completely well.

The principal reason for treating patients with osteomyelitis of the neck of the femur by conservative means has been the difficulty in early diagnosis and of surgical attack, with the added factor that so far patients so treated have done better than those who underwent operation.

On the basis of this limited experience we do not recommend conservative treatment in all cases of osteomyelitis of the neck of the femur in patients at this age. We do recommend, however, that if the patient is carefully observed, a conservative attitude may be taken, and frequently surgical procedure may be avoided. If there is evidence that the process ruptures into the joint, the joint should be drained, or if there are other indications for operation, it should be carried out.

COMMENT AND CONCEPTION OF TREATMENT

In contrast with the osteomyelitis of older persons is the osteomyelitis of infants, with its relatively brief duration, infrequent sequestration and rare recurrences. To what do we ascribe these differences?

They are due in part to the fact that Staph. aureus is less frequently present in this group. Staph. aureus is a destructive organism whether it involves soft tissue or bone and produces sequestration more often than Str. haemolyticus in patients of any age,[5] but there is not so striking a difference as there was in this series.

It is our opinion that certain anatomic and physiologic features in bones themselves are a considerable factor. Osteomyelitis in general may be considered "a cellulitis of bone," with death of tissue from the direct activity of the infection and from disturbances of the vascular supply, which seem to be in part mechanical. The necrosis causes the extensive sequestration seen in dense cortical bone.

In the bones of infants certain factors militate against this occurrence. In infancy the vascular spaces are larger and the bone is of spongy texture, even in the so-called compact portion, as suggested by Bardeen;[6] the bony tissue has a much larger soft tissue element and generally less rigidity. This construction allows freer communication between the marrow and the subperiosteal spaces and thus provides a mechanism for a decompression by which the pus from the juxta-epiphyseal area and marrow cavity is able to pass to the subperiosteal space. Ordinarily osteomyelitis has its origin in the metaphysis (fig. 10), and Starr's[7] opinion was that the infection passes from there through the thin cortical bone and appears subperiosteally. It may be seen in figure 9 that although the cortical bone is thinner at the metaphysis than elsewhere in older children, it is particularly thin in

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6. Bardeen, C. R.; Keibel, F., and Mall, F. P.: Manual of Embryology, Philadelphia, J. B. Lippincott Company, 1910.

7. Starr, C. L.: Acute Hematogenous Osteomyelitis, Arch. Surg. 4:567 (May) 1922; Acute Infections in Bone, in Robert Jones Birthday Volume, London, Oxford University Press, 1928, p. 183.

infants. This allows in infants a free communication from the original site of the osteomyelitis to the subperiosteal space. The periosteum is more loosely attached in infants and further aids in the decompression. The roentgenograms of the patients in this series suggest extensive subperiosteal dissection, if one may judge from the distribution of new bone. It is the usual thing for subperiosteal new bone to be evident from one half to the full length of the shaft, and, as may be seen in figure 11, this reaction extends down the shaft much farther than the involvement of the cortical bone and marrow space.

Once the pus is beneath the periosteum, the periosteum may rupture without sequestration, as occurred in 26 of our cases in which operation

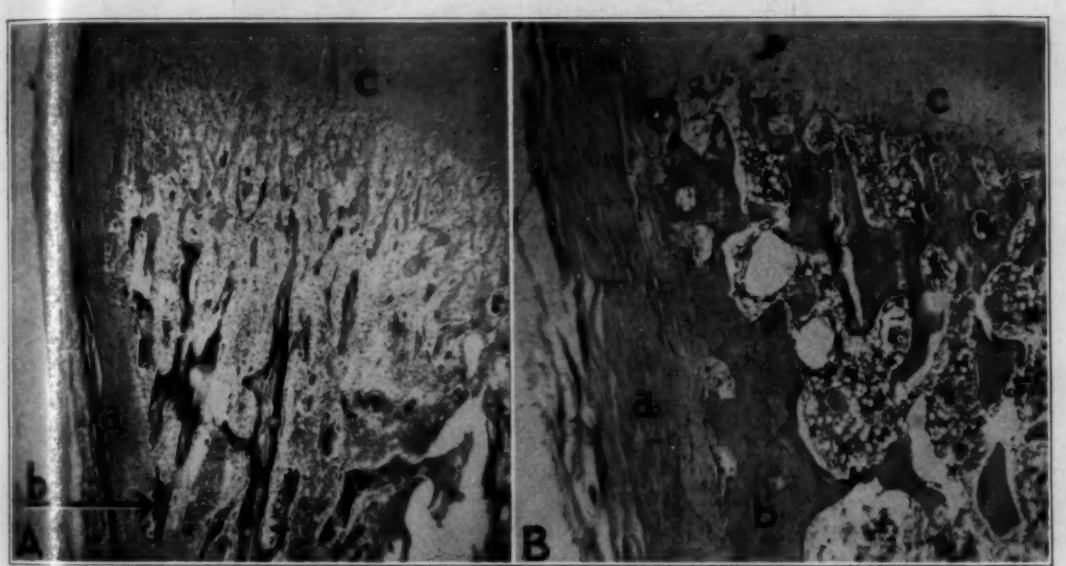

Fig. 9.—Photomicrograph of normal ribs at the metaphysis (*A*) in a premature infant and (*B*) in a child of 11 years. In *A* note that little cortical bone (*b*) is present at the metaphysis, allowing a rather direct communication between the marrow and the subperiosteal spaces. The cortical bone in the remainder of the shaft shows relatively larger haversian canals than are seen in older persons. There is a contrast with *B*, in which there is a relatively thick layer of cortical bone (*b*) at the metaphysis, although even at this age the cortical bone at the metaphysis is relatively thin as compared with the remainder of the shaft. In this illustration *a* indicates periosteum, *b*, cortical bone, and *c*, the epiphyseal line. Hematoxylin and eosin; approximately × 30.

was not performed until after the periosteum had ruptured. In other words, there is an orderly decompression by nature without gross sequestration except in rare instances.

Further factors which seem to explain the rapid healing of the lesions and the infrequency of sequestration are suggested by histologic

examination of the involved bones. What necrotic bone there is is rapidly absorbed by a process of autolysis (fig. 12). Incidentally, osteoclasts are conspicuously infrequent where this process is taking place. The formation of new bone in the process of healing is remarkably rapid in infants. This is seen not only in the roentgenograms but particularly in microscopic sections of involved bone, in which as soon as a week after the onset subperiosteal new bone may be noted in many instances (figs. 10, 11 and 12). In other words, not only is the dead

Fig. 10.—Photomicrograph of the lower end of the femur adjacent to the metaphysis in a 1 month old infant, showing an osteomyelitic process of two weeks' duration. Note the necrosis and beginning absorption of the trabeculae (*d*), the thin cortical bone (*b*), areas of cellular infiltration of the acute inflammatory type (*e*) and the surrounding subperiosteal new bone (*f*). Hematoxylin and eosin; approximately × 30.

bone rapidly absorbed, but the process of healing is equally rapid. This combination of a natural method of decompression with the additional factors of rapid absorption of the necrotic bone and equally rapid healing would seem to serve as an explanation for many of the differences between the disease of infants and that of older persons.

Ordinarily a patient with cellulitis, generally speaking, does better when the process is allowed to localize than when it is incised early, particularly if the infection is streptococcic. On this basis there are

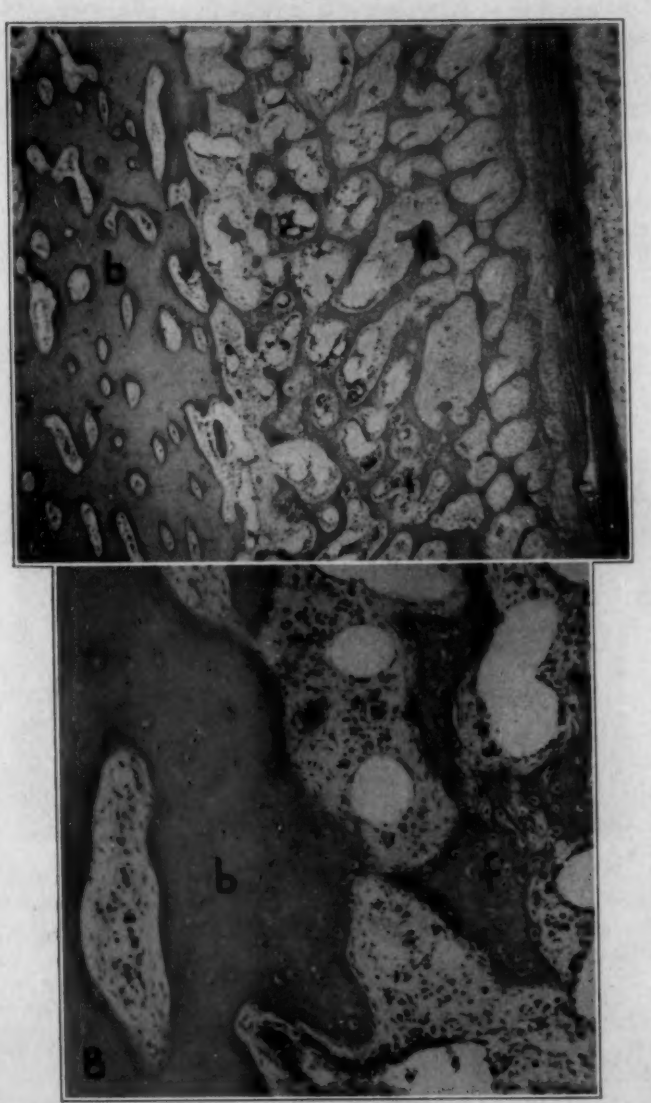

Fig. 11.—*A* is a photomicrograph of the midshaft of the same bone as that seen in figure 10. Note the extensive layer of subperiosteal new bone (*f*) surrounding the living bone of the shaft (*b*). The subperiosteal new bone extends much farther down the shaft than the involvement of the cortical bone. Hematoxylin and eosin; approximately × 30. *B* is the same as *A* in higher magnification (approximately × 83). Hematoxylin and eosin.

many, though they are greatly in the minority, who advocate waiting as a general rule. The decision depends on balancing the argument between the possible danger of operating on an early diffuse inflammatory process and that of allowing an infection to progress in rigid walls, with resultant increased necrosis of bone. As far as infants are concerned, and clinically it has seemed that the age of 2 years is a flexible but fairly definite dividing line between infancy and childhood, the importance of the latter is greatly minimized. Infants have a natural method of decompression which works effectively, with sequestration a rare accompaniment. Certainly the evidence suggests that waiting for localization should do little harm.

Fig. 12.—Photomicrograph of osteomyelitis of the fibula of nine days' duration in an infant of 1 year and 2 months. Note the autolysis of the necrotic bone (*b*) as surrounding subperiosteal new bone (*f*) is laid down. The area indicated by *g* is an artefact, i. e., separation in preparation. Hematoxylin and eosin; approximately × 30.

This is fortunate, for the accurate determination of the site of an early lesion in a child of this age is difficult. Without this exact determination, many needless and harmful surgical procedures may be undertaken, particularly if the child is desperately ill or there is a complicating infection of the respiratory tract.

In recent years it has not been our chief concern to operate on the patient at the earliest possible moment, particularly if the site of the lesion cannot be definitely localized or there is some contraindication to operation from the general condition of the patient. We have fol-

lowed the practice of immobilizing the part, usually with poulticing, and of giving general supportive therapy. Almost without exception the children have improved following this regimen. Once the site of the lesion is definitely recognized and the child is considered a good surgical risk or at least the possibility of improving his condition for operation is no longer present, one should consider operation. However, in many instances in our series we deliberately waited until the abscess became localized and fluctuation was palpable before carrying out a simple drainage of the abscess, without any operative procedure on the bone. It being remembered that the immediate danger of the acute disease is the foremost consideration with young patients, this attitude allows a minimal amount of surgical trauma and permits the time of operation to be chosen with full consideration of the patient's condition. The patients in these cases have done very well, and the course compares most favorably with that in the others. In none of them has there been sequestration or has the sinus failed to heal within four months. Neither has the incidence of sepsis of the joints been greater, although more cases must be observed to determine this point with finality.

Whether this method of allowing localization of the abscess with simple drainage is preferable to making a window in the bone at an earlier time, we cannot say. In any event, if the abscess is drained a prolonged search for the lesion in the bone should not be made nor should the operative procedure be complicated in order to make a window in the bone.

The way in which the infection has been taken care of in the cases in which conservative treatment was followed further aids one's conception of the disease in infants. Mild, acute osteomyelitis may take care of itself without drainage following immobilization; occasionally this is true in cases in which the patient is severely ill.

Postoperative Care.—It is our usual practice to pack the wound with petrolatum gauze and immobilize the part with a plaster cast which is bivalved. The wound is not dressed until granulations have formed, so that the dressing may be accomplished without trauma, in other words, from seven to fourteen days after the operation. Dressings are then done at about weekly intervals, with replacement of the petrolatum gauze, until it can no longer be introduced. At this time a rubber tissue dressing is used, which keeps the margins of the wound moist, facilitates drainage and obviates too early closure of the external orifice of the sinus. In our experience this regimen is less odoriferous and more conducive to prompt healing than the unmodified regimen of Orr.[8]

Immobilization.—An essential part of our preoperative and postoperative regimen is immobilization of the part, as may be seen in the

8. Orr, H. Winnett: Osteomyelitis and Compound Fractures, St. Louis, C. V. Mosby Company, 1929.

reports of representative cases. Case 7 particularly illustrates the value of protecting the part, in that when the traction was removed on two occasions there was an exacerbation of the symptoms. Not only do we feel the importance of immobilization as a preoperative and immediate postoperative measure, but we consider that the part should be immobilized until the sinus has healed and there is definite evidence in the roentgenogram that the bone is healing. The only exception to this rule occurs when there is secondary involvement of the joint.

Our mortality rate has been gradually decreasing under this regimen. There has been only 1 death in the last 20 cases, and that was in an infant 3 weeks of age with primary omphalitis, Staph. aureus septicemia, multiple visceral abscesses and involvement of six bones.

SUMMARY

Ninety-five cases of osteomyelitis in infants (children under 2 years) are reported on, 35 of which have been observed in the last two years. In 82 the condition was acute and in 13 chronic (i. e., duration over one month at the time of the admission to the hospital).

Osteomyelitis in infants is not a rare disease.

The mortality rate for all cases was 21 per cent. The rate was definitely higher in patients under 6 months of age (43 per cent). The rate in patients from 6 months to 2 years of age was 14 per cent.

Streptococcic osteomyelitis occurs twice as frequently as staphylococcic osteomyelitis in infants.

Antecedent infections were present in 55 per cent of the cases. Fifty per cent of the complications were infections of the respiratory tract; 25 per cent were cutaneous lesions, and the other 25 per cent were such miscellaneous infections as omphalitis and chickenpox.

When associated with infection of the respiratory tract, osteomyelitis was due usually to Str. haemolyticus, occasionally to Pneumococcus and rarely to Staph. aureus. When associated with cutaneous lesions the organism was more likely to be Staph. aureus.

There was a history of mild trauma in 17 per cent of the cases.

In the entire group of cases of acute osteomyelitis there was a higher mortality rate with staphylococcic than with streptococcic infections, whereas in infants under 6 months of age streptococcic osteomyelitis caused a relatively higher rate.

A diagnosis is made later in the course of the disease in cases in infants than in those in older persons.

Differential diagnosis demands the particular consideration of sepsis of the joints, infection of the soft tissues and scurvy with infection elsewhere.

The average duration of hospitalization was six weeks.

The average period required for the sinus to close was twelve weeks.

Sequestration is rare in infants. Sequestrectomy was necessary in only 6 cases. Roentgen examination frequently reveals marked destruction of the shaft with an extensive involucrum, suggesting that sequestration will occur, but this rarely happens.

If the patient survives the acute infection, the prognosis for sound bones is excellent. Recurrence almost never occurs. In only 1 of the 41 cases in which a follow-up study recently was made did examination reveal the lesion in the bone to be not clinically healed, and this was a recent case. In 1 other case the roentgenograms suggested a smoldering lesion, but there had been no symptoms since the sinus had healed.

There was residual deformity in 5 cases, mainly caused by involvement of joints.

Seventy-one patients with acute osteomyelitis were operated on. In 37 an operation on the bone was performed, usually the formation of a window; in 34 drainage of the secondary abscess or periosteal incision was performed.

The cases in the two groups showed little difference in the immediate or the final prognosis, but the comparison is inaccurate because the cases in the two groups were not comparable.

In 8 cases of acute osteomyelitis treatment was by immobilization without operation. Five patients were mildly ill, and 1, moderately ill; these 6 patients recovered completely. Two patients were critically ill, with osteomyelitis of the neck of the femur and septicemia; 1 completely recovered and the other is recovering. In none did a sinus develop.

Of the 6 patients with osteomyelitis of the neck of the femur, the 3 not operated on and treated by immobilization with constant observation did better than those on whom drainage was established by surgical intervention.

It is suggested that the differences between the osteomyelitic syndrome of infants and that of older children are largely dependent on three factors: (*a*) The organism, Streptococcus, is observed more frequently in infants than in older children. (*b*) The anatomic construction of the bone in infants, characterized by larger cancellous spaces in the bone, allows the infection to pass more readily from its site of origin, the metaphysis, to the subperiosteal space; the periosteum is more loosely attached in the infant and allows the decompression to occur; the periosteum then ruptures, allowing the pus to escape into the soft tissues, without sequestration except in rare instances. (*c*) The absorption of dead bone occurs more rapidly in infants, as does the formation of new bone.

The therapy we have adopted is based on the following considerations:

(*a*) The care of the patient rather than the osteomyelitis is the important consideration.

(*b*) Surgical intervention at an early period in the disease is not essential. If the condition of the patient is satisfactory and the lesion can be located definitely before operation, an operation may be performed.

(*c*) If surgical intervention is contraindicated by the general condition of the patient, the part should be immobilized and supportive treatment should be given. Delay does not increase the danger of sequestration, which is remote in any instance, and particularly so if the offending organism is Streptococcus.

(*d*) If an operation is performed on the bone it should not be extensive.

(*e*) Adequate drainage of the fluctuant abscess in infants, without operation on the bone, seems to give as satisfactory results as a more extensive procedure. If the abscess is drained a prolonged search for the lesion in the bone should never be made.

(*f*) Packing the wound open with petrolatum gauze combined with immobilization in a plaster cast is a desirable method of treatment. The cast should be bivalved to allow for dressings. The first dressing should not be made until ten days after the operation, thus allowing granulation tissue to line the wound. At that time dressing can be done painlessly. Dressings are done at weekly intervals thereafter with replacement of the petrolatum gauze.

(*g*) The part should be immobilized until the wound has healed and there is evidence of healing in the roentgenogram.

Since this therapy was instituted our mortality rate has greatly decreased There has been only 1 death in the last 20 cases.

CONCLUSION

Osteomyelitis of infants differs greatly from osteomyelitis of older children, not only in many clinical features but also in many principles of therapy.

NOTE.—Since this paper was prepared, we have seen an article by Paschlau,[9] in which the author pointed out differences between the osteomyelitis of infants under 1 year and that of older children. He contrasted the pathologic process and certain clinical features of the

9. Paschlau, G.: Die Besonderheiten der Osteomyelitis im frühen Kindersalter, Monatschr. f. Kinderh. **55**:280, 1932.

disease in infants with those in older children. He mentioned the frequent incidence of septic joints and displacement of the epiphysis. He expressed the opinion that incision and drainage of the abscess are generally sufficient. The mortality rate in his series was 38 per cent.

For statistical purposes only we have utilized the cases of 41 patients treated by the surgical service of Dr. W. S. Ladd, at the Children's Hospital.

IMMUNOLOGY OF OSTEOMYELITIS

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Hematogenous osteomyelitis is considered a surgical problem. It is our belief that antecedent to the presenting surgical problem of acute osteomyelitis is the fact that susceptibility to this infectious process depends on the presence or the absence of immunologic defenses in the host. These defenses are the preeminent factors in susceptibility, acuteness and chronicity, and they may determine the mortality and the tendency to recurrence.

In the hands of experienced surgeons operative technic has reached a supreme degree of perfection. No one questions that surgical intervention for osteomyelitis is frequently a life-saving procedure and markedly shortens the course of the chronic infection. In the face of these facts the incidence of osteomyelitis remains the same, and the percentage of recurrences in properly handled cases still remains high. This evidence warrants a study of the immunology of this infectious process in an attempt to throw some light on the problem of susceptibility and of recurrence.

This paper is confined to a consideration of hematogenous osteomyelitis. In over 90 per cent of the cases the staphylococcus is the invading organism and is obtained in pure culture. Pigment-producing strains predominate. Let it be recalled that in every case osteomyelitis is at its inception a bacteremia. The blood in a majority of cases eventually sterilizes itself, with the localization of the invading bacteria in certain bones. If the infection is virulent and the body defenses are inadequate, multiple bones may become involved with a recurrence of bacteria in the blood.

When one attempts to estimate accurately the percentage of deaths due to acute osteomyelitis, a wide discrepancy of individual statistics is noted. However, a compilation of statistics gathered from various competent observers places the mortality at approximately 10 per cent. From the registration area of the United States during the years 1930, 1931 and 1932, 3,160 deaths were reported from osteomyelitis.[1] It is significant that 90 per cent of the deaths occur within the first two weeks

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From the Contagious Service of the Kansas City General Hospital, in collaboration with the Department of Orthopedic Surgery.

1. Bureau of the Census, Mortality Statistics, 1930, 1931, 1932, Washington, D. C., Government Printing Office.

of the disease. This fact must be interpreted as indicating a lack of a defensive mechanism within the host, for once the host has had ample time to elaborate immune substances, the mortality drops sharply.

Most observers concede that osteomyelitis develops subsequent to some minor abrasion or staphylococcic infection occurring in the skin. Antecedent trauma is frequently an important factor in the anatomic localization of the disease. From this frequently minor port of entry in the skin the organism invades the blood stream and is hematogenically borne to the bone. When this blood-borne deposit of bacteria produces the characteristic signs of inflammation, the first localizing symptoms of osteomyelitis are manifest.

The staphylococcic flora of the normal skin is extensive. All types are found with regard to both the ability to produce pigment and the power to hemolyze blood. There is much evidence which shows that the saphrophytic staphylococci of the healthy skin are capable of producing a hemolytic exotoxin, and in acute lesions of the skin this power of hemolysis is more marked. This fact in itself would indicate that on the intact skin may be found virulent staphylococci living as saphrophytes, but following trauma or minor infections these potentially virulent staphylococci may become invasive and capable of producing deep lesions.

In our study of seventy-one strains of staphylococci obtained from patients with severe infections studied to date, sixty-four showed a demonstrable toxin, and in seven instances no toxin-making properties could be demonstrated. Theoretically one can postulate that invasion of the human body occurs only from potentially virulent staphylococci of the cutaneous flora.

Since furuncles are frequently a precursor of osteomyelitis, the comparative percentages in the table are of interest:

Results of the Study of Strains of Staphylococci Obtained From Patients with Severe Infections

Type of Infection	Total Number of Cases	Hemolysis		Necrosis		No Hemolysis		No Necrosis	
		Number of Cases	Percentage	Number of Cases	Percentage	Number of Cases	Percentage	Number of Cases	Percentage
Osteomyelitis	27	24	88.8	22	81.4	3	11.2	5	18.6
Furuncle	19	17	89.5	14	73.7	2	10.5	5	26.3
Pyemia	4	4	100	4	100				
Cellulitis	3	2	66.6	2	66.6	1	33.3	1	33.3
Vegetative bacterial endocarditis	4	4	100	3	75	..	....	1	25
Cavernous sinus thrombosis	4	4	100	4	100				
Carbuncle	5	4	80	3	60	1	20	2	40
Pyoderma gangrenosum	1	1	100	1	100				
Abscess of the brain	1	1	100	1	100				
Necrotizing ulcers complicating erysipelas	3	3	100	3	100				
Totals	71	64	90.1	57	80.5	7	10.5	14	19.5
Acne	5	..	....	..	....	5	....	5	

Van de Velde [2] first demonstrated that certain strains of staphylococci produced leukocidin, which in all probability is identical with the exotoxin and which has properties both to hemolyze blood and to necrose tissue. Much of the early work was done by Burnett [3] in Australia and by Parker [4] in New York. Of late this exotoxin has received a great deal of attention, particularly by the English investigators. We shall not attempt to elaborate on the history of the development of the knowledge concerning the toxin.

In recovering the toxin from staphylococci it is necessary to have a dextrose-free medium and care should be taken that the p_H of the medium is adjusted and that the organism is grown under reduced oxygen tension. We shall not discuss the technical bacteriologic process by which this toxin is demonstrated but shall merely state that the toxin can be demonstrated in a filtrate so obtained which is sterile to culture both aerobically and anaerobically.

Many filtrates produce hemolysis with no necrosis, but we have not encountered a nonhemolytic filtrate which showed necrotic properties. To a degree, the power of hemolysis is an index to dermonecrosis. The necrotic property of a potent toxin frequently is found to be 7,000 dermonecrotic units per cubic centimeter of toxin. It is quite common to find a toxin which will hemolyze washed rabbit cells in a dilution of 1:1,280. Evidently this toxin has a dermonecrotic and hemolytic component in variable amounts. By injection of the toxin intravenously or intracutaneously into experimental animals, death may be produced in from a few hours to several days, depending on the amount of toxin injected and on its potency. By attaching an electrocardiograph and a pneumograph to a dog which previously had received lethal doses of staphylotoxin, Nelis and Bouckaert [5] showed that death was caused by ventricular fibrillation, with an attendant progressive fall in blood pressure. Animals dying after several days of toxemia show definite histologic changes, especially in the heart, kidneys and liver. That the death, necrosis and histologic changes in these cases are due to the exotoxin of the stphylococcus and not to histamine is well authenticated by the work of Dolman,[6] who stated: "Histamine has been shown to

2. Van de Velde, H.: Étude sur le mécanisme de la virulence du Staphylocoque pyazène, Cellule **10**:401, 1894.

3. Burnett, F. M.: Exotoxins of Staphylococcus Pyogenes Aureus, J. Path. & Bact. **32**:717 (Oct.) 1929.

4. Parker, J. T.: Production of Exotoxin by Certain Strains of Staphylococcus Aureus, J. Exper. Med. **40**:761 (Dec.) 1924.

5. Nelis, P., and Bouckaert, J. J.: Action cardiaque de la toxine staphylococcique chez le lapin et chez le chien, Compt. rend. Soc. de biol. **113**:1157, 1933.

6. Dolman, C. E.: Pathogenic and Antigenic Properties of Staphylococcus Toxin, Canad. Pub. Health J. **23**:125 (March) 1932.

be present in the original broth. Such amounts of histamine could not possibly be responsible for any of the characteristic features of the toxin. Moreover, if the histamine content of the toxin be destroyed by incubating it with histaminase the original properties of the toxin remain unimpaired." Moreover, this toxin forms a toxoid when treated with formaldehyde.

It has long been suspected that in osteomyelitis a free toxin is present and that many of the symptoms are attributable to an existing toxemia. Postmortem examination of patients dying within the first two weeks of the disease shows histologic changes pointing to a condition of extreme toxemia. These findings are not unlike those in the rabbit subjected to lethal doses of staphylotoxin, as evidenced by the following histopathologic report.

The section of cardiac muscle of a rabbit depicted in figure 1 shows alternate dark-staining muscle fibers and light-staining muscle fibers. The light-staining fibers show considerable longitudinal fibrillation. The darker muscle fibers show peculiar obliteration of the striations, with no perivascular infiltration about the blood vessels. The microscopic diagnosis was toxic myocardial degeneration.

The section of the kidney of a rabbit shown in figure 2 reveals considerable exudate in the capsule of Bowman, marked by light-staining coagulated protein with compression of the capillary tufts. The proximal convoluted tubules show marked cloudy swelling and more or less desquamation of the tubular epithelium. The passive congestion is more or less marked. All tubular structures show evidence of a varying degree of cloudy swelling. There are no interstitial changes and no marked round cell infiltration. The microscopic diagnosis was acute parenchymatous degeneration with glomerular exudate.

The outstanding feature in the liver of a rabbit a section of which is shown in figures 3 and 4 is a large thrombus in the branch of the portal vein. In the immediate environ of this thrombus is a large area of necrosis, demarked sharply from living liver cells. The liver cells in the viable area are well stained and show no marked deviation from the normal. In some of the portal canals round cell infiltration is marked. The blood vessels show marked passive congestion of the liver columns. In general they are arranged well and not broken up by central necrosis. The microscopic diagnosis was thrombotic necrosis of the liver with round cell infiltration.

The muscle fibers of the human heart, shown in figure 5, are of small diameter and are richly nucleated. The blood vessels are widely dilated. A high power view reveals poorly developed cross-striation of fibers, which take a deep eosin stain and show considerable cloudy swelling. There are no other material changes. Here and there are small foci of round cell infiltration of muscle fibers and extravasation of blood into the fibers. The microscopic diagnosis was acute congestion of the muscle of the heart with evidence of infective inflammation.

Figure 6 shows much necrotic coagulation in the tubules of this human kidney. Marked passive congestion is present everywhere. The glomeruli are swollen generally, occupying the capsules of Bowman tightly. The passive congestion in many parts has proceeded to the passage of blood in the tubular structures. All the tubules are involved in a necrotic process. There is cast formation in the tubules

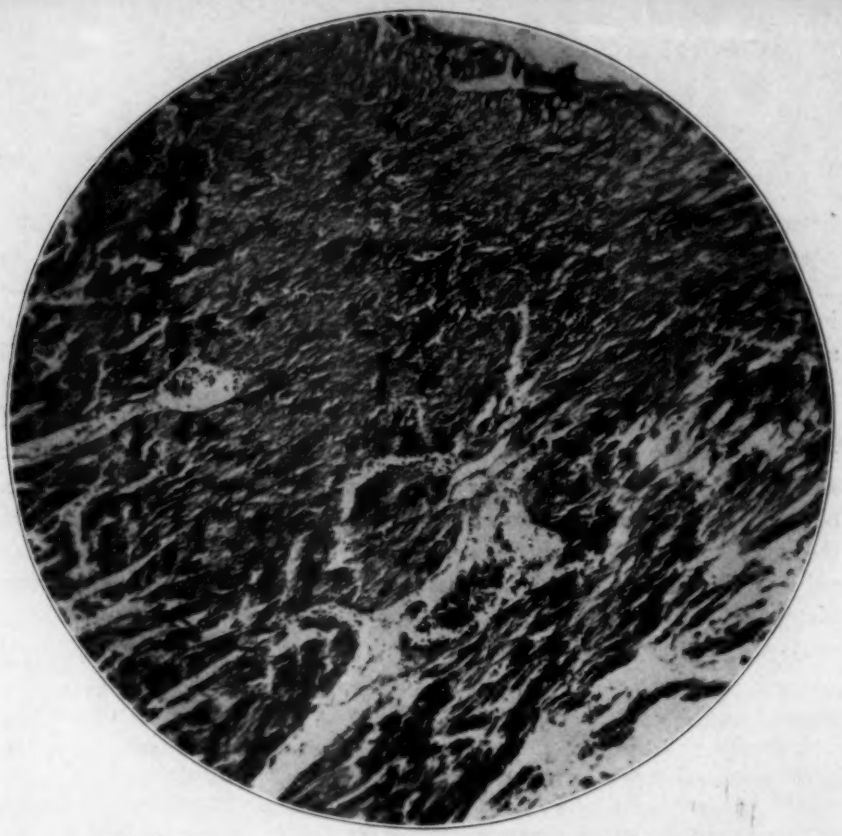


Fig. 1.—Low power photomicrograph of the heart of a rabbit.

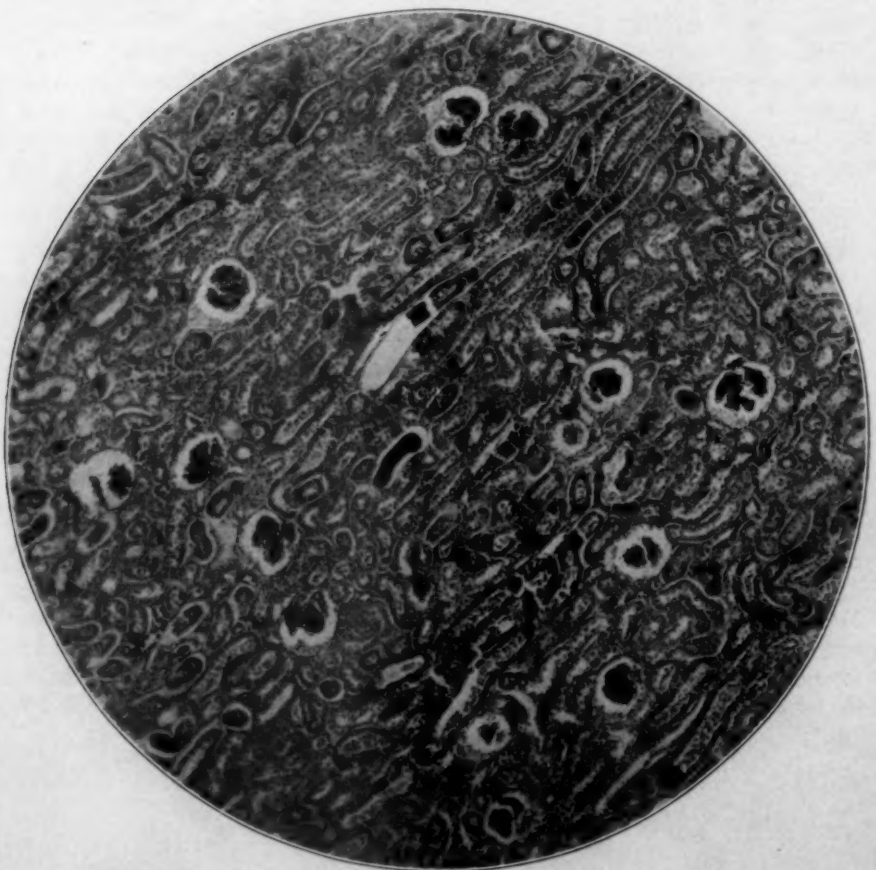
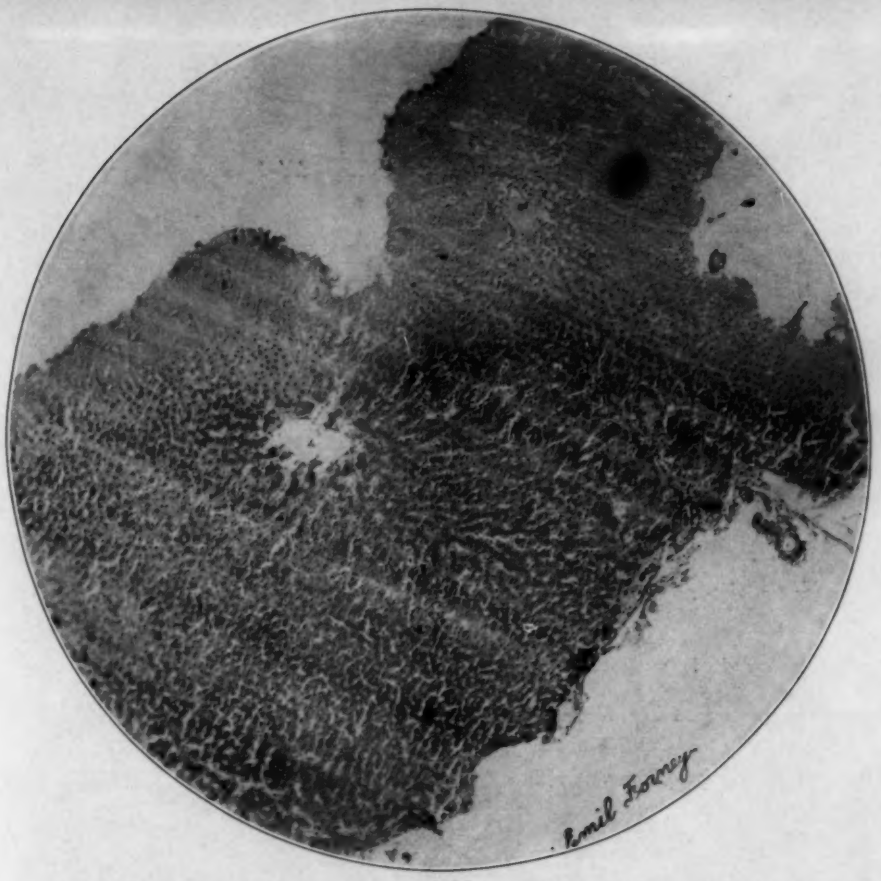
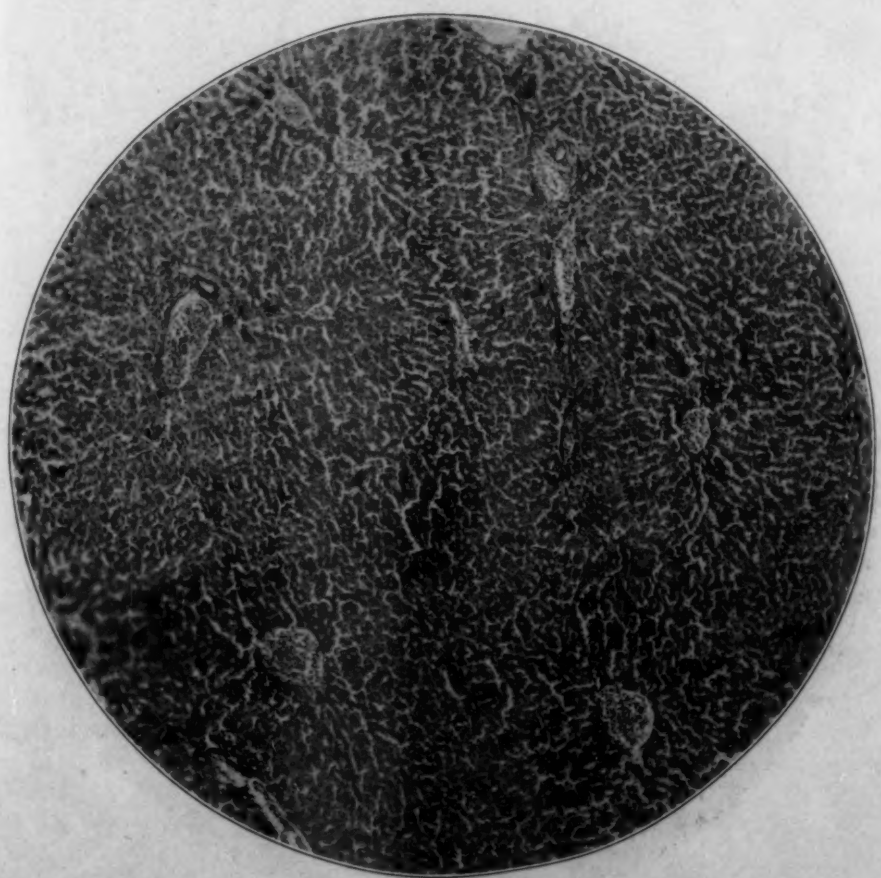


Fig. 2.—Low power photomicrograph of the kidney of a rabbit.





Figs. 3 and 4.—Low power photomicrographs of the liver of a rabbit.

Fig. 5.—Low power photomicrograph of the human heart.

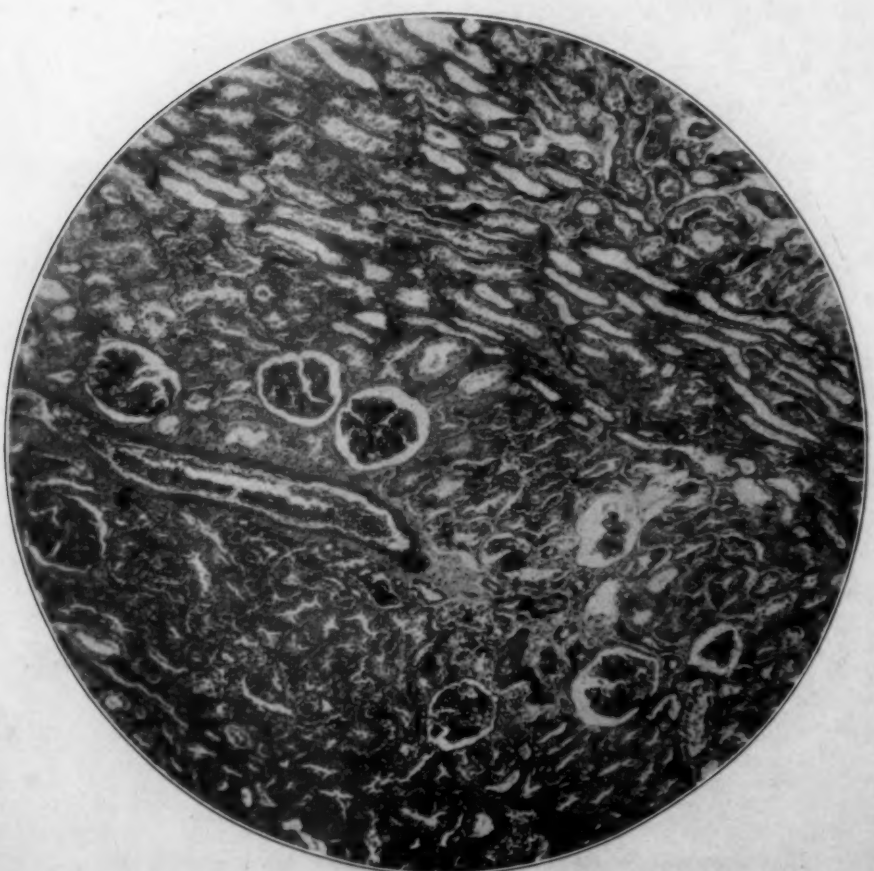


Fig. 6.—Low power photomicrograph of the human kidney.

in fair abundance. The microscopic diagnosis was extreme renal congestion with necrosis of the tubular epithelium, most marked in the proximal convoluted tubules.

The human liver depicted in figure 7 shows an advanced degree of passive congestion. The columns of liver cells are reduced in breadth by congestion of the blood vessels of the sinusoids of the liver. A few spots show the beginning of fibrous tissue formation. The portal canals show marked round cell infiltration. The Kupffer cells are increased in number and contain hemosiderin pigment. The microscopic diagnosis was subacute hepatitis with marked congestion and round cell infiltration.

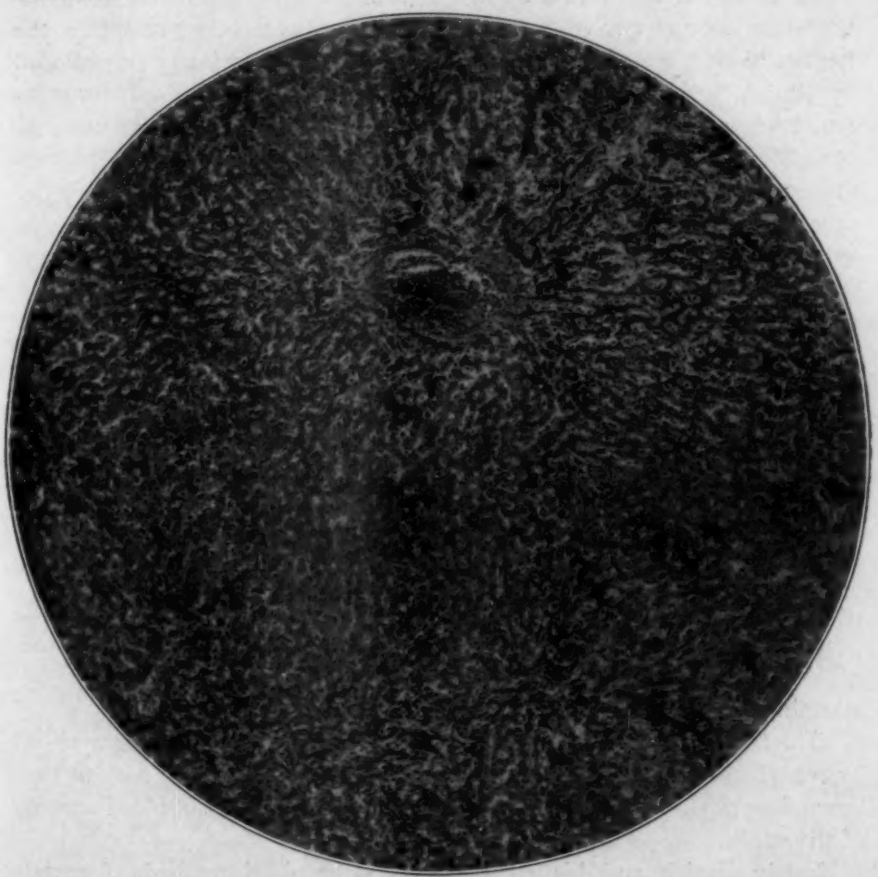


Fig. 7.—Low power photomicrograph of the human liver.

We have to date studied the toxin-forming properties of twenty-seven strains of staphylococci obtained from cases of osteomyelitis. It is interesting to note that in twenty-nine cases of osteomyelitis the staphylococcus was isolated twenty-seven times. Of the twenty-seven cultures, twenty-four were hemolytic, twenty-two necrotic, three non-hemolytic and five non-necrotic. If one considers hemolysis as evidence of the formation of toxin, this would mean that in twenty-seven cases of staphylococcic osteomyelitis twenty-four of the invading organisms were

toxin makers. These organisms were obtained from persons with acute hematogenous osteomyelitis or with an acute recurrence at the time of operative procedure. No culture was utilized from draining sinuses.

From experiments in immunization conducted on rabbits and other experimental animals with the staphylococcus toxin, it was found that the laboratory animal requires approximately two weeks to make an immune response to the free staphylococcus toxin used as an antigen. Also, from the fact that antitoxic substances against the free toxin of the staphylococcus have been shown to be consistently present in the human blood serum by Neisser and Wechsberg,[7] and lately emphasized by Parish, O'Meara and Clark,[8] one must assume that staphylococcus antitoxin is one of the defenses of the body against the invasion of toxigenic staphylococci. Clinically this is supported by the observation that in osteomyelitis the blood stream sterilizes itself at approximately the time required for the human organism to respond to the staphylotoxin antigen. One must remember that over 90 per cent of the deaths that occur from acute staphylococcic osteomyelitis take place within the first two weeks of the disease, before the body has had ample opportunity to elaborate antitoxic substances. These clinical observations support the laboratory observations that the antitoxin in the blood is of importance in the defense against these toxigenic staphylococci.

It is not uncommon to find that the most virulent toxin-making staphylococci may be isolated from a person with osteomyelitis of minor clinical severity. This is evidence that the defenses of the body are able to cope with this infection, and one finds a high titer of antitoxin in the blood taken from these patients. Conversely, severe osteomyelitis may be present in a person who shows little antitoxic titer in his blood. Staphylococci isolated from such patients may show but a slight degree of toxin-making property although the clinical symptoms may be alarming.

The beneficial results obtained in the treatment of acute osteomyelitis by transfusion of blood from an adult donor may be due in part to the titer of staphylococcus antitoxin consistently present in the blood serum of the adult.

Lately Parish and his collaborators determined methods for the measurement of the antitoxin content of the blood. Unfortunately at the present time there is no generally accepted standard of procedure, and each worker utilizes a different standard of measurement; the results therefore necessarily become comparative.

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7. Neisser, M., and Wechsberg, F.: Ueber das Staphylotoxin, Ztschr. f. Hyg. u. Infektionskr. **36**:299, 1901.

8. Parish, H. J.; O'Meara, R. A. Q., and Clark, Winnifred H. M.: Clinical Investigation of Staphylococcal Toxin, Toxoid and Antitoxin, Lancet **1**:1054 (May 19) 1934.

In the study of the blood of one hundred persons of unknown history in our laboratory, the staphylococcus antitoxin titer was measured and found to average 1 : 16. In the measurement of the antitoxin of persons suffering from chronic osteomyelitis, the titer was found to be as high as 1 : 4,000, but the average was found to be many times the normal. The following tabulation shows the antihemolytic titer of normal persons and of those with osteomyelitis (the asterisk indicates recurrence of osteomyelitis one week after the measurement of the titer).

Dilution.....	No.	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512	1:1,024	1:2,048	1:4,096
Blood of normal persons.....	100	21	31	30	13	4	1	0	0	0	0	0
Blood of persons with osteomyelitis.....	26	0	0	1*	6	3	0	2	4	4	4	2

The technic of the measurement of the antitoxin content of the blood as developed by Parish is based on the ability of the free antitoxin of the blood serum to be bound to a known quantity of staphylotoxin, a suspension of washed rabbit cells being used as an indicator. If the toxin is in excess, hemolysis will take place. The end-point is marginated sharply.

Commercial staphylococcus antitoxin now available for experimental use according to our method of measurement shows an antihemolytic titer approximately 700 times that of ordinary blood serum. Commercial manufacturers standardize antitoxin by its power to neutralize a definite number of dermonecrotic doses of toxin per cubic centimeter of antitoxin. A potent staphylococcus toxin will measure about 5,000 to 7,000 dermonecrotic doses per cubic centimeter. The rabbit, because of its low natural antitoxin titer is the animal of choice for this measurement. The standard antitoxin will neutralize 100,000 dermonecrotic doses of toxin per cubic centimeter. This antitoxin is the concentrated pseudoglobulin fraction of horse serum, in which fraction the immune substances are carried.

In a study of the immunology of osteomyelitis, several factors present themselves. We found in a summary of three hundred cases of osteomyelitis that the youngest patient encountered was 3 months of age, the average age being 13 years. The low age incidence of this disease suggests an accidental factor coupled with a low incidence of immunity in childhood against virulent staphylococci, which are commonly present on the normal healthy skin as saphyrophytes. Evidence is rapidly accumulating that the titer of natural antitoxin present in the blood plays an important part in the protection of the host against this infection.

The high titer of available staphylococcus antitoxin immediately suggests the possibility of therapeutic attainments by the use of this

antitoxin in an attempt to procure passive immunization. The fact that the immune titer of antitoxin is infinitely higher than that of ordinary adult blood used in transfusion in an effort to combat toxemia and destruction of blood should indicate that this procedure is worthy of serious consideration. Pronounced early anemia, so frequently observed, is strong presumptive evidence that the invading organism is toxigenic with marked properties of hemolysis. That the natural antitoxin does not appear in great quantities until after the second week of the infection, together with the fact that the majority of deaths from osteomyelitis occur within the first two weeks of the disease, indicates that the optimum time for antitoxin therapy is early in the course of the infection. This contention is supported by the fact, as previously mentioned, that material obtained post mortem from patients dying early in the course of the disease and from rabbits dying from lethal doses of toxin shows marked toxic degeneration, particularly in the heart, kidney and liver. Once the blood stream has become sterile, with the process localized in the bone, and the body defenses have reacted to the antigen, there is, in our judgment, little to be hoped for from the administration of antitoxin. In the light of the present knowledge, we can only say that staphylococcus antitoxin will neutralize the free toxin fraction. We have on repeated occasions actively immunized rabbits, by the use of staphylotoxin, against several times the lethal dose of toxin. Animals inoculated with virulent living staphylococci live longer when antitoxin is administered. In a series of rabbits receiving living staphylococci one half of those which were treated with staphylococcus antitoxin showed a slightly lower mortality than the controls which received no antitoxin.

The possibility of active immunization has received some attention, since the fact has become known that staphylococcus toxin which has been treated with formaldehyde and incubated at 37 C. for a period of days forms toxoid which has antigenic properties. The advisability of using vaccines in an attempt to create active immunity is not attended with unanimity of opinion. Our experience in conjunction with a study of the available reports in the literature indicates that unquestionably the use of staphylococcus toxoid raises the immune titer in man as well as in laboratory animals.

The problem of recurrence in osteomyelitis is yet to be elucidated. It is possible that recurrences may be associated with a fall in the immune titer of the blood, which is familiarly spoken of as lowered resistance. At the present time all our attempts to measure the titer of immune substances in chronic osteomyelitis have shown a high degree of protective substances. It is our opinion that the defensive substances of the blood measured over a long period of time may disclose valuable information relative to the relapse in the patient who has had osteomyelitis.

The therapeutic use of staphylococcus antitoxin in acute osteomyelitis and attempts to vaccinate the patient with chronic osteomyelitis by the use of toxoid will be the basis of further reports.

CONCLUSIONS

Of 27 cases of osteomyelitis of staphylococcic etiology, a free toxin was demonstrated in 88.8 per cent.

Of 44 cases of deep staphylococcic lesions exclusive of osteomyelitis, a free toxin was demonstrated in 91 per cent.

There is a resident titer of antitoxin against staphylococcus toxin in normal adult blood serum.

In chronic osteomyelitis this immune titer is markedly increased.

In the treatment of acute staphylococcic osteomyelitis a donor known to have a high antitoxic titer should be procured.

Dr. Ralph Emerson Duncan granted the cooperation of the laboratory and the use of its facilities and Dr. Frank J. Hall interpreted the pathologic and histologic specimens. The Lederle Laboratories supplied the antitoxin and some of the cultures.

A HISTOLOGIC STUDY OF MECKEL'S DIVERTICULUM

WITH SPECIAL REFERENCE TO HETEROTOPIC TISSUES

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The recent literature contains numerous references to gastric mucosa adjacent to the so-called "peptic ulcers of Meckel's diverticulum." In these articles interest is almost entirely restricted to the clinical aspects of the anomaly. My purpose in this paper is to report the histologic observations in nineteen new cases of Meckel's diverticulum and to collect the previous data on the incidence, position and types.

The first case of Meckel's diverticulum mentioned in the literature is that of J. H. Lavater in 1672. In 1698 Ruysch referred to this diverticulum, and in 1701 he published an illustration of an additional case. Littre in 1742 observed such a diverticulum in a hernia. However, until the time of Meckel little was known of the diverticulum which bears his name. In 1808 he mentioned it, and in 1812 he wrote the first accurate description of the diverticulum, giving its embryologic background and emphasizing its clinical importance. In this connection it is interesting to note that as far back as 1769 Morgagni stated that he had observed in several instances a diverticulum on the intestine of a goose.

MATERIALS

The material used in this investigation consisted of nineteen diverticula, ten of which were supplied by Dr. J. S. Horsley of St. Elizabeth's Hospital, Richmond, Va. Five operative specimens and three autopsy specimens came from the Laboratory of Pathology of the University of Virginia Hospital. Nine of the specimens (cases 1 to 9) from Dr. Horsley were of the usual type with a lining of mucosa typical of that seen in the small intestine, with numerous cells of Paneth. The specimen in case 10 was unusual in that it had numerous protrusions. The five operative specimens from the University of Virginia Hospital included two with an area of gastric mucosa; the three autopsy specimens included one with such an area. The nineteenth specimen came from Dr. T. P. Bagwell of Grace Hospital, Welch, W. Va. This specimen was ulcerated and contained a patch of gastric mucosa.

Except where otherwise indicated, slides were made from the tip of the diverticulum, because without exception when the position of the heterotopic tissue was noted in the literature it was always found in the

From the Laboratory of Histology and Embryology, University of Virginia.

apex. In the case of an unusual diverticulum, slides were made from all parts. All the specimens were stained with hematoxylin and eosin as a routine measure, and all were embedded in paraffin and cut into sections at intervals of 7 or 10 microns.

CASES 1 to 9.—The diverticula in this group were of the usual type with mucosa like that of the ileum. The specimens need not be described further.

CASE 10.—The diverticulum was supplied by Dr. Horsley. It was a sausage-shaped mass, 17 by 10 mm. From various parts of its surface projected seven protrusions which varied in size and were irregularly placed. The diverticulum was connected to the ileum by a very small stalk. Approximately eighty slides were made of this diverticulum, and the sections were so spaced as to show parts from the whole specimen.

Microscopically, the specimen was found to contain typical intestinal mucosa with very distinct goblet cells and villi. The protrusions were plainly seen in certain of the sections. They consisted of a lining epithelium, which was continuous with that of the diverticulum and an outer lamina muscularis mucosae. In one section, especially, it was very easy to see that the epithelium, the lamina muscularis mucosae and the lamina propria of the protrusion were continuous with that of the diverticulum. Outside of the mucous membrane of the protrusion was a layer of areolar tissue which contained numerous blood vessels. This seemed to be continuous with both the submucosa and the fibroserous coat of the diverticulum. The muscular coat stopped short at the lateral border of each protrusion, so that the delicate lamina muscularis mucosae constituted all the muscular tissue found in the protrusion. Neither the diverticulum nor any of its protrusions were inflamed. Moderate numbers of Paneth cells were present.

CASE 11.—The specimen was obtained at autopsy on a young man and was supplied by the department of pathology of the University of Virginia. The diverticulum was situated 100 cm. from the ileocecal valve. Macroscopically, it was a pouch, wider at the neck than at the tip, and measured 55 by 25 mm. No gross lesions were visible. Microscopic study was based on sections taken from seven regions. In the tip of the diverticulum an area estimated to be from 3 to 4 mm. in diameter was found to contain gastric mucosa. The gastric mucosa was from two to three times as thick as the intestinal mucosa. It contained tall, clear pink-staining columnar cells. In the tunica propria could be seen the fundic glands, with both chief and parietal cells visible. However, the parietal cells were not especially numerous. Paneth cells were numerous in the fundus of the glands of the intestinal mucosa.

CASE 12.—The specimen was removed by Dr. Bruce Morton in the course of an appendectomy on Mr. K. B. The gross pathologic report from the pathologic department stated: "The specimen was 5 cm. in length, consisting of a pouch, the open end of which was intestinal wall. The distal end was bulbous and irregular and somewhat firmer. In cut section the mucosa appeared normal. In the distal end the mucosa was piled up to entirely fill the lumen." The bulbous mass at the distal end was 15 mm. long, and there was some ulceration and inflammation.

As seen in microscopic sections, the mucosa of the distal end was very thick and thrown into folds. The lining epithelium of these folds was made up of tall columnar cells which stained faintly pink. In certain areas beneath these columnar cells could be seen typical fundic glands, with the chief and parietal

cells clearly visible. In other areas the glands beneath this epithelium seem less differentiated, and parietal cells could not be made out. Such areas were presumably pyloric. In many areas intestinal and gastric glands were mixed. Eosinophils were especially numerous throughout the mucosa of the diverticulum.

Case 13.—The specimen was obtained at autopsy from Miss M. P., aged 23, and was supplied by the department of pathology of the University of Virginia. It measured 6 by 2.5 by 2 cm. Microscopic study revealed typical intestinal mucosa. The cells of Paneth were especially prominent, frequently lining the entire tip of the fundus of the intestinal glands.

Case 14.—The specimen was obtained at operation and was supplied by the department of pathology of the University of Virginia. Its dimensions were 3.5 by 2 by 1.5 cm. Microscopically, a subacute inflammatory condition was found. There was a purulent exudate in the lumen, and the mucous membrane was infiltrated with polymorphonuclears and lymphocytes. Most of the diverticulum was lined with mucosa like that seen in the small intestine. An area about 1 cm. in diameter had clear, faintly pink-staining columnar cells. Under these there was marked infiltration, but in a few areas parietal cells could be identified.

Case 15.—The specimen was obtained at autopsy and was supplied by the department of pathology of the University of Virginia. Microscopic study disclosed mucosa like that seen in the small intestine and many cells of Paneth in the base of the intestinal glands.

Case 16.—The specimen was obtained at operation and was supplied by the department of pathology of the University of Virginia. Gross examlnation revealed marked inflammation and ulceration. On microscopic examination an inflamed and eroded mucous membrane of the type seen in the small intestine was found, with a small number of the cells of Paneth present in the bases of some of the intestinal glands.

Case 17.—The specimen was removed at operation from Mr. C. F., and was obtained from the department of pathology of the University of Virginia. Gross examination disclosed that the diverticulum measured 3.8 by 2.1 by 2.6 cm. and that the mucosa of the tip appeared swollen.

Microscopic examination revealed gastric mucosa of the fundic type throughout most of the diverticulum. This consisted of tall, clear, pink-staining columnar cells lining the ducts of the gastric glands. The fundus of the glands was quite long, and typical chief and parietal cells were found. The muscularis mucosae was doubled in the gastric portion, and in one area under the gastric mucosa the muscularis consisted of three layers. An area of pyloric mucosa was found. In this area the parietal cells were few and scattered, and the gastric crypts were deep. In one portion of the submucosa there was a mass of pancreatic tissue 8 mm. in diameter. There were well developed ducts, and although islets were present they were difficult to find.

Case 18.—The specimen was removed from Miss M. H. P. at the time of operation for salpingectomy. It was obtained from the department of pathology of the University of Virginia. The mucosa was of the type characteristic of the ileum (fig. 1).

Case 19.—The specimen was removed from a young man by Dr. T. P. Bagwell at Grace Hospital, Welch, W. Va. Preoperatively, the condition was diagnosed as a perforated duodenal ulcer, but at operation a perforated Meckel's diverticulum was found. After preservation in 95 per cent alcohol, the specimen measured 45 by 30 mm. A small clearcut ulcer 5 mm. in diameter could be seen.

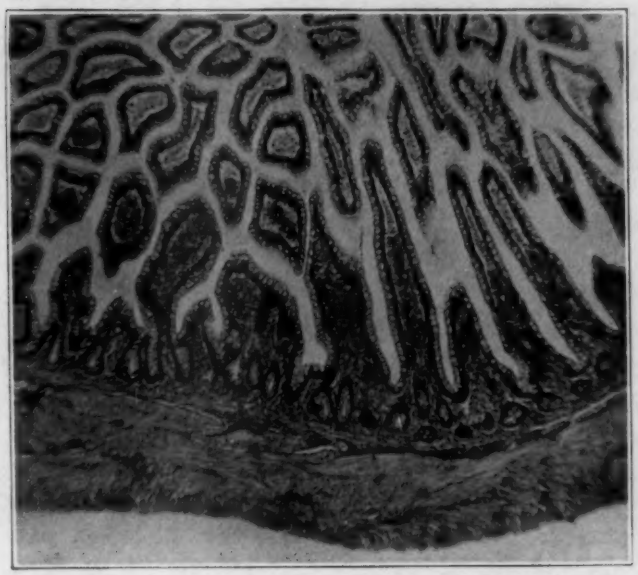

Fig. 1 (case 18).—Transverse section of the wall of Meckel's diverticulum, showing tall typical villi and short intestinal glands (× 96).

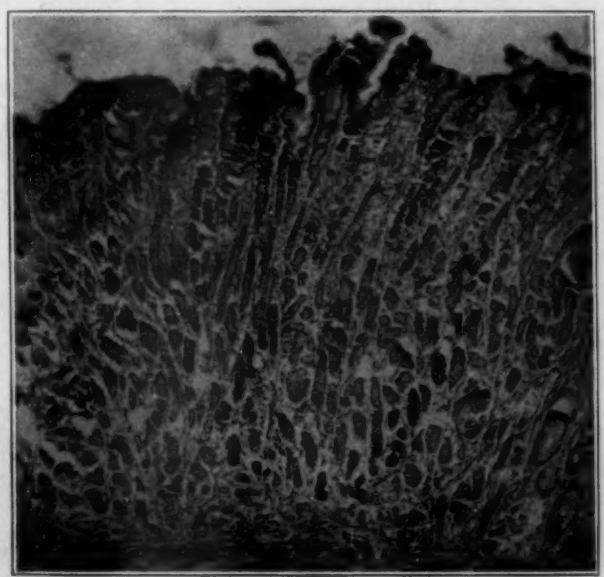

Fig. 2 (case 19).—Vertical section of the gastric mucosa of the apical portion of Meckel's diverticulum, showing typical fundic glands (× 96).

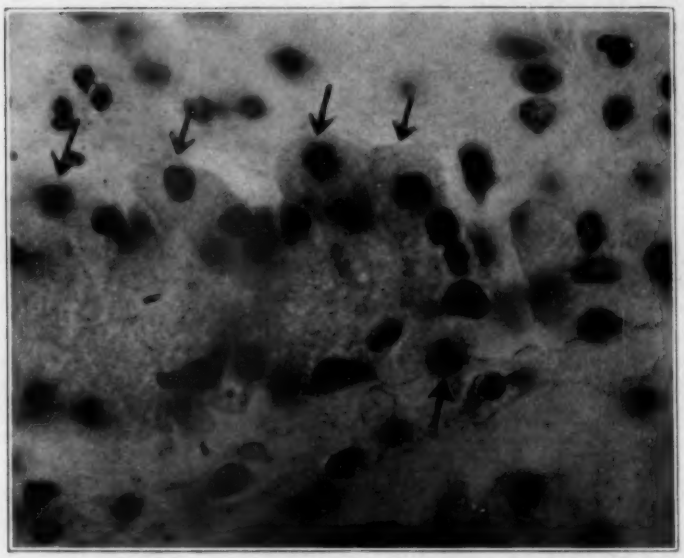

Fig. 3 (case 19).—Portion of a fundic gland from figure 2, showing the parietal cells (× 1,000).

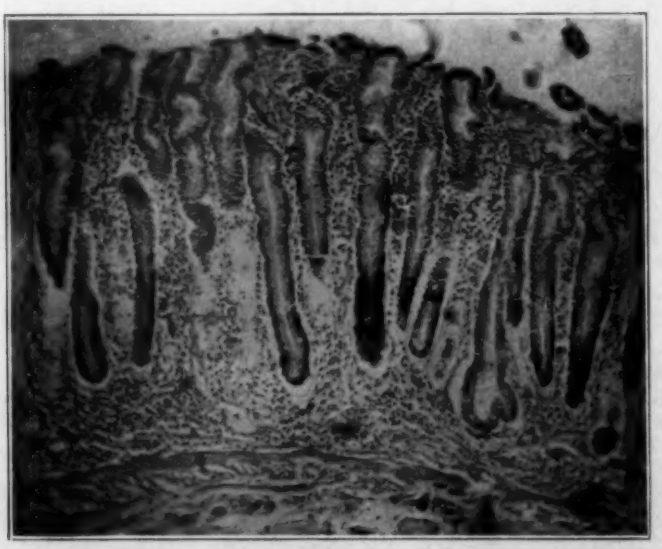

Fig. 4 (case 19).—Vertical section of the mucosa of Meckel's diverticulum adjacent to the area of figure 2, showing long intestinal glands similar to those of the colon except for fewer goblet cells. Between these two areas occurs a narrow region with short stout villi and long intestinal glands with many goblet cells (× 96).

TABLE 1.—*Data in Cases of Meckel's Diverticulum With Gastric Mucosa, Compiled From the Literature* *

Date	Author	Sex of Patient	Type of Mucosa
1903	Hilgenreiner	M	? (not recorded)
1904	Koch	? (not recorded)	Fundic
1906	Hildebrandt	F	?
	Koch	?	Pyloric
1907	Deetz	M	?
1909	Kohlmeyer	?	?
	Koch	?	Pyloric
1912	Koch	?	Pyloric
	Koch	?	Fundic
	Koch	?	Fundic
1913	Hübschmann	M	Fundic
1915	Callender	?	Fundic
	Gramen	M	Fundic
1918	Meulengracht	M	Fundic
1919	Goetsch	M	Fundic
	Müller	M	Fundic and pyloric
1920	Barron	M	Fundic
1922	Mégevand and Dunant	M	Fundic and pyloric
1923	Schaetz	M	Fundic and pyloric
	Schaetz	M	?
	Stone, Eric	M	Fundic
	Nicholson	M	Fundic
1924	Hallopeau and Humbert	M	?
	Guibal	M	Fundic
	Brasser	M	Fundic
1925	Schaetz	M	Pyloric
	Schaetz	M	?
	Schaetz	F	?
	Schaetz	M	?
	Schaetz	M	?
	Schaetz	F	?
	Schaetz	M	Fundic, pyloric and cardiac
	Pascale	F	?
	Ulrich	M	?
1926	Etchegorry	?	?
	Kleinschmidt	M	Fundic
	Moll	?	?
1927	Abt and Strauss	F	?
	Jackson	M	Fundic
	Büchner	M	Fundic
	McCalla	M	Fundic
	Taylor	M	Fundic
	Taylor	M	Fundic and cardiac
	Taylor	M	Fundic
	Taylor	M	Fundic
	Taylor	F	Fundic
	Gramen	M	?
	Gramen	F	?
	Meiss	?	?
1928	Hartglass	F	Fundic
	McMurrich and Tisdall	M	Fundic and pyloric
	Peterman and Seeger	M	Fundic
1929	Franke	?	?
	Winkelbauer	M	?
	Winkelbauer	M	?
	Treplin	?	?
1930	von Haberer	M	Fundic
	von Haberer	F	Fundic and pyloric
	Aschner and Karelitz	M	Fundic
	Aschner and Karelitz	F	?
	Febre, Patel and Lepart	M	?
	Green	M	Pyloric
	Schmidt	M	?
	Edwards	M	Fundic
1931	Lindau and Wulff	M	Fundic
	Greenwald and Steiner	M	?
	Greenwald and Steiner	M	?
	Büchner	F	Fundic
	Christie	?	?
	Cobb	M	Fundic
	Debre, Bopp and Semelaigne	M	?
1932	Roudil and Marty	F	?
	Singer and Vaughan	M	?
	Royster, H. A.	?	?
	Mason and Graham	M	Fundic
	Hudson and Koplik	?	? (9 cases)
	Hudson	?	Fundic (2 cases)
	Hudson	?	Pyloric
	de Vernejoiel	M	?
	Schaaff	M	Fundic
1933	Smith and Cohen	M	?
	Hudson and Koplik	?	? (6 cases)
	Dragstedt	?	Fundic
	Mayo, C. W.	M	?
	Miller and Wallace	?	?
	Clark, D. F.	M	Fundic
	Boch, H.	M	?
1934	Hunt and Bonesteel	M	Fundic
	Schullinger and Stout	M	?

89 cases

* References to the cases cited in this and in the following tables are to be found in the bibliography.

Serial sections were made of the area about the ulcer. The rest of the diverticulum was cut into sixteen pieces, and slides were made from each piece.

Microscopically, the ulcer appeared to be subacute. The peritoneal surface about the ulcer showed a marked inflammatory reaction with a thick layer of leukocytes and fibrin and an attempt at organization of the exudate. The ulcer was surrounded by intestinal mucosa. An area about 1.6 mm. from the ulcer (as measured by serial sections) showed gastric mucosa typical of that seen in the fundus. On microscopic examination of the slides of the rest of the diverticulum it was noted that the distal fourth of it was lined with gastric mucosa (fig. 2). The gastric mucosa was from four to five times as thick as the intestinal mucosa of the proximal part. The fundus of the glands was from six to seven times as long as the ducts. In the fundus typical chief and parietal cells were found. The parietal cells were quite numerous (fig. 3). The ducts were lined with tall, columnar, clear, faintly pink-staining cells. No Paneth cells were found in any of the sections which revealed intestinal mucosa. A small area of the mucosa surrounded by typical intestinal mucosa with villi had the appearance of the mucosa of the colon (fig. 4).

TABLE 2.—*Data in Additional Cases of Umbilical Polyps and Fistulas with Gastric Mucosa, Compiled from the Literature*

Date	Author	Sex of Patient	Type of Mucosa
1880	Gould	? (not recorded)	? (not recorded)
1881	Tillmans	?	?
1887	Roser	M	?
1888	van Heukelom	?	Pyloric
1889	von Rosthorn	?	Pyloric
1898	Reichard	?	?
	Weber	?	Pyloric
	Lindner	?	Pyloric
1899	Lexer	?	Pyloric
1903	Strada	?	Pyloric
1904	Salzer	?	Cardiac
1905	Minelli	?	Gastric adenoma
1908	Denuce	?	Fundic
1911	Negroni	?	?
1922	Nicholson	?	?
1923	Stone, Eric	?	?
	Nicholson	?	Fundic and pyloric
1925	Taylor	?	Fundic
1931	Lindau and Wulff	?	?
1933	Hudson and Koplik	?	?

CASES REPORTED IN THE LITERATURE

Data in cases of Meckel's diverticulum with gastric mucosa, compiled from the literature, are presented in table 1.

Hilgenreiner, while not stating that his specimen contained gastric mucosa, published an illustration of a diverticulum in which the distal end had a much thickened mucosa which was probably gastric in nature.

Since umbilical polyps and fistulas are also remnants of the vitelline duct, a list of the cases of these conditions with gastric mucosa is included (table 2).

Kustner described some columnar cells which he thought came from the urachus in an umbilical adenoma. From the illustration they look somewhat like gastric glands.

COMMENT

While it has been known since 1861 that pancreatic tissue may occur in Meckel's diverticulum, the knowledge of the occurrence of gastric mucosa is of comparatively recent date (1904). That this gastric mucosa is active in producing a secretion similar to, if not identical with, the gastric juice of the stomach and containing both pepsin and hydrochloric acid has been shown several times in cases in which gastric mucosa has been seen at the umbilicus in polyps and fistulas (Telling, Stone, Taylor, Lexer, Hudson and von Rosthorn), and in a Meckel's diverticulum (Schaaff). Such polyps and fistulas are, like Meckel's diverticulum, anomalies resulting from failure of the vitelline duct to undergo normal involution at about the 7 mm. embryonic stage. It is therefore reasonable to assume that the gastric mucosa found in Meckel's diverticulum is also quite active in secreting pepsin and hydrochloric acid and that this secretion increases at mealtime, just as that in the stomach and umbilical fistulas is known to do. Such a secretion comes at a time when the small intestine and Meckel's diverticulum are relatively empty and the alkaline intestinal juice is not being formed. The acid gastric juice can accordingly act on the intestines undiluted, and it is not remarkable that ulcers are not uncommonly associated with this aberrant gastric mucosa. This is the explanation advanced by Lindau and Wulff for the formation of these ulcers.

Hudson and Koplik found that 67 per cent of their diverticula contained gastric mucosa. All their specimens were pathologic, and there can be little doubt but that the presence of much gastric mucosa is certain to be associated with some pathologic change. Their percentage, accordingly, must be higher than for the general incidence. Koch in 1912 found that six of fifty diverticula examined contained gastric mucosa; Schaetz in 1925 noted gastric mucosa in five of thirty specimens studied. In the nonpathologic specimens collected for this report there is gastric mucosa in but one of fourteen diverticula examined. The average of the last three series indicates an incidence of about 13 per cent.

Although the presence of pancreatic tissue in Meckel's diverticulum has been recognized for about seventy years, its occurrence is not very common. The only available statistics on the incidence of this aberrant tissue in this location are those of Schaetz, who found pancreatic tissue in three of thirty diverticula examined, and Koch who found it in two of fifty specimens. An average of these two series gives an incidence of 6.3 per cent, which seems too high in view of the relatively infrequent reference to such a condition in the literature.

The primitive digestive tube consists of an endodermal epithelial lining and a layer of mesoderm forming the splanchnopleure. Originally the cells of this endoderm are structurally identical throughout and from them are developed in the fetus the epithelial lining of all the parts of

the digestive tract from the pharynx to the rectum and all the glands associated with this tract, with the possible exception of the parotid gland. In Meckel's diverticulum alone almost all of the differential potentialities of this endoderm may be realized.

TABLE 3.—*Reports of Duodenal Glands in Additional Data on Meckel's Diverticulum*

Date	Author	Additional Data
1897	Kern	
1906	Hedinger	Pancreatic tissue also
1909	Tschiknawerow	
1912	Koch	
1925	Schaetz	Male; gastric mucosa also
1930	Fevre, Patel and Lepart	Male
1932	Hudson and Koplik	
	McCann	Male; pancreatic tissue also
1933	C. W. Mayo	Gastric mucosa also
1934	Schullinger and Stout	Gastric mucosa also

TABLE 4.—*Reports of Pancreatic Tissue in Meckel's Diverticulum*

Date	Author	Additional Data
1861	Zenker	
1870	Neumann	
1891	Schmauser	
1893	Schirmer	
1899	Brünner	
1901	Wright	Islets
	E. Albrecht	Islets
1904	Bize	
1905	Merkel	
	Deve	
1906	Hedinger	Duodenal mucosa also
1907	Deetz	Male; gastric mucosa also
1908	Clogg	
	Kothe	Man
1909	Nazari	
	Busch	
1910	Albrecht and Arzt	
1911	Tschiknawerow	
1912	Koch	Two cases with gastric mucosa also
	Drummond	Female
	Sil	
1916	Cullen	
1922	Cullen	
1925	Schaetz	Male; islets present
	Schaetz	Female; islets and gastric mucosa
	Schaetz	Male; fundic, pyloric and cardiac glands also
	Steiger	
1927	J. B. Stone	
	Taylor	Three cases, all with gastric mucosa and islets
	Winkelbauer	Male; gastric mucosa also
1928	Cogniauz	
1932	Hudson and Koplik	
	Mason and Graham	Male; gastric mucosa also
	McCann	Islets and duodenal glands
1934	Hunt and Bonesteel	Male; gastric mucosa and islets

The investigators listed in table 3 have reported duodenal glands in cases of Meckel's diverticulum.

Investigators who have found pancreatic tissue in cases of Meckel's diverticulum are listed in table 4.

The type of mucosa characteristic of the colon has been reported in Meckel's diverticulum by Hudson and Koplik (two cases) and by Stern.

Von Rosthorn found tissue which to him resembled that of the parotid gland in a case of umbilical fistula. The occurrence of such tissue is difficult to explain, since the parotid gland is probably of ectodermal origin. It is possible that what he found was really pancreatic tissue.

As both islets and acini come from the same primordia, it is not surprising that several authors have specifically mentioned finding islets in the aberrant pancreas.

Case 11, that of the specimen with protrusions, while not without precedent in the literature, is unusual. Cullen collected reports of several cases of what he termed hernial protrusions. This term is particularly apt in view of the microscopic study of my case, in which the mucous membrane lacks a muscular coat and looks as if it might have pushed its way through this layer. Cahill described a diverticulum with three "tit-like projections on it." Kelynach found several specimens with "secondary lateral dilations" and some with "nipple-shaped projections." Doepfner published five illustrations of diverticula showing projections.

Practically every type of anomaly resulting from failure of all or part of the vitelline duct to become obliterated has been described. In some cases the distal part of the duct fails to atrophy, which results in an umbilical fistula or polyp. In rarer cases the whole duct fails to retrogress, and a patent umbilical fistula results. Sometimes Meckel's diverticulum has a thin fibrous strand attached to its distal end where atrophy started but was incomplete. This fibrous strand may be free in the abdominal cavity, or attached at the umbilicus or attached to some abdominal organ.

Giant diverticula, while rare, are reported in the literature. Diverticula over 50 cm. long have been described (McMurrich and Tisdall, Edmunds, Moll and Edwards), as well as one which filled almost half of the abdomen (Yates). McMurrich and Tisdall expressed the belief that certain of these large diverticula represent the remains of both the vitelline duct and the yolk sac. It is thought that the persistent stalk and sac are drawn into the abdomen by the intestines when they return from the celom of the umbilical cord. Christie and Doepfner reported terminally bifurcated diverticula.

In addition to the stomach and Meckel's diverticulum, other portions of the gastro-intestinal canal have been described as having at least in part a lining of gastric mucosa. Nicholson stated that cardiac epithelium is found in 75 per cent of persons in the esophagus at the level of the cricoid cartilage. This same investigator stated that in some cases inflammation in various parts of the intestinal tract causes a metaplasia of the epithelium resulting in the formation of gastric glands. In support of this theory he offered the evidence from seventeen cases in which a gallbladder removed for cholecystitis or cholelithiasis contained mucous

glands of the gastric type, three cases of tuberculous ulceration of the intestines which showed gastric glands in the area about the ulcer and one case of a pancreatic cyst which was in part lined by gastric mucosa. Poncher and Milles found two tumors in the mediastinum of an infant. These tumors were presumably of enterogenous origin, and in the case of each there was noted a small area of gastric mucosa. In this same infant the small intestine was reduplicated in the lower part. The reduplication opened into the intestine 20 cm. above the ileocecal valve but ended blindly. This blind end was found to be lined with gastric mucosa of the fundic type.

The actual autopsy reports do not bear out the figures usually given for the occurrence of Meckel's diverticulum. Table 5 contains a list of reports collected from the literature on this subject. It is really a

TABLE 5.—*Incidence of Meckel's Diverticulum as Found in the Literature*

Source of Data	Number of Cases of Meckel's Diverticulum	Number of Autopsies
Kelynach	18	1,446
Schmidt	14	1,822
Mitchell	39	1,635
Hilgenreiner	33	1,767
Augier	4	200
Augier	1	100
Testat, 1888	16	769
Testat, 1892	4	298
Rogie	8	400
Boston City Hospital	11	1,382
Johns Hopkins Hospital	15	2,600
Dresden City Hospital	8	8,133
Anatomic Society of Great Britain and Ireland	16	769
Bender Hygienic Laboratory	5	953
Turner	81	10,360
Sandlos	14	1,300
Baby Hospital	63	5,768
Schaetz	17	737
Total	367	40,439

collection of several series of statistics, and in only a few cases was the original article available. All the available figures on the subject have been included in order to get a large enough number to give an adequate basis for reliable estimation.

The average incidence in this table is about 0.9 per cent. Figures given by other writers are: Adami, 2.7 per cent; Fuchsig, 2 per cent; Coleman, 1.8 per cent; Harbin, 2 per cent, and Abt and Strauss, from 1 to 3 per cent.

The statement usually made with reference to the sex incidence of Meckel's diverticulum is that it occurs three times as often in the male as in the female. It is of interest to note that eight of the ten specimens submitted by Dr. Horsley were from females and none contained gastric mucosa. An average of all the figures that could be collected on the subject seem to bear this out (table 6).

Doepfner's figures give one diverticulum each in one hundred and two males and two hundred and fourteen females. Hilgenreiner placed the figure at one in sixty-one females and thirty-nine males.

As some of the foregoing data come from autopsy reports, and since in general more males are brought to necropsy than females, this figure is perhaps a little too high. However, when the figures from the operating room are studied, where the numbers of patients of the two sexes are more nearly equal, there remains little doubt that Meckel's diverticulum occurs more often in males than in females. This disproportion in sex distribution of gastric mucosa in cases of Meckel's diverticulum accords roughly with that for gastric and intestinal ulcers.

The only instance in the series reported here in which the position of the diverticulum was determined was one in which it was situated 100 cm. above the ileocecal valve. This is the upper limit as given by most authors. Foerster gave the upper limit as 4 feet (121.9 cm.) above

TABLE 6.—*Distribution of Meckel's Diverticulum as to Sex*

Author	Male	Female
Schaetz	9	8
Kettler	91	18
Mitchell	35	4
Christie	50	13
Hudson and Koplik	30	15
Wellington	201	64
Kelynach	11	7
Sandlos	5	9
Total	432	138
Proportion	3.1	1

the cecum. Fitz placed the position at 12 inches (30.5 cm.) above the valve in the new-born and 3 feet (91.4 cm.) in the adult. In Kelynach's eighteen cases the upper limit was 50½ inches (128.8 cm.); the lower limit, 15 inches (38.1 cm.), and the average, 34½ inches (87.6 cm.), which is approximately the figure that is usually given for its position, namely, 3 feet. In Hudson and Koplik's series of thirty-two cases the diverticula ranged from 8 to 40 inches (20.8 to 101.6 cm.) above the ileocecal valve. Christie, in a series of sixty-three cases, found the upper limit to be 90 cm. above the cecum; the lower limit, 15 cm., and the average, 50.6 cm.

The question arises as to how these heterotopic growths in the remnants of the vitelline duct are to be explained. Since gastric mucosa was first found in the umbilicus, the earlier attempts at explanation were concerned with aberrant tissue in this location.

Tillmanns in 1882 first found gastric mucosa at the umbilicus. He looked on this mucosa as the remains of a gastric diverticulum which projected through the umbilicus and the connection of which with the

stomach was severed by the primitive rotation of the stomach. Weber, Reichard and Roser accepted this view.

Van Heukelom in 1888, after examining a series of embryos, expressed himself as being unable to understand how a diverticulum from the stomach could possibly get to the umbilicus in view of the fact that a large liver is between the stomach and the umbilicus at the stage when the vitelline duct is supposed to atrophy (7 mm. stage, 38 days). In one of his fetuses he found an area of gastric mucosa connected with Meckel's diverticulum but not in communication with its lumen. Because of this lack of communication, he postulated that there was a substance in the intestines which stimulated the intestines to form intestinal mucosa and the lack of which was necessary to the formation of gastric mucosa. He assumed that this substance was bile. This view has recently been supported by the discovery of a similarly placed area of gastric mucosa in a strand of tissue between the ileum and the umbilicus by Barron. However, so many cases of gastric mucosa in Meckel's diverticulum in free communication with the lumen of the ileum have been found that the theory of van Heukelom cannot in its entirety be true.

Salzer in 1904 proposed the theory that irritation and inflammation stimulated the endoderm to grow in a manner foreign to that particular region. There is perhaps an element of truth in his view also, although there are many cases in which gastric mucosa appears in diverticula that do not seem to be inflamed. However, in every case in which the position of the aberrant tissue is stated, it is always at the apex, where the vitelline duct begins to atrophy and to constrict. Whatever causes this atrophy and constriction certainly would cause some irritation to the underlying endoderm. If such irritation actually were present in the embryo its influence could easily be outgrown.

Albrecht and Fischl look on this gastric mucosa as arising from misplaced fetal inclusions or rests. This view is similar to that offered in explanation of many foreign growths. In recent years Schaetz has been the chief proponent of this theory. Such a theory is difficult to prove or disprove. However, if the theory is true it seems strange that except in Meckel's diverticulum, were gastric mucosa has been reported many times, no cases (Taylor) have been reported in which congenital gastric mucosa has been found below the duodenum. Apparently other factors must be concerned.

Taylor in 1927 found some gastric mucosa in the ileum 10 inches (25.4 cm.) from the ileocecal valve. He emphasized the fact that it was located on the mesenteric side, which fact he believed proves that it is not a part of Meckel's diverticulum. In view of its embryologic formation one would, of course, expect the remains of the vitelline duct to be found on the antimesenteric side, as is usually the case. However,

McMurrich and Tisdall described several cases which suggest that it can arise from the mesenteric border. They mentioned the case of Robertson which has not yet been reported, in which the diverticulum arose from the ileum on its mesenteric side 20 cm. from the ileocecal valve. Edmunds reported a case in which the diverticulum ran 40 cm. through the mesentery. In an 18 year old girl, Reed found a diverticulum which arose from the mesenteric border of the intestine. Abt and Strauss found a diverticulum which was located between the layers of the mesentery and which arose from the mesenteric border. Accordingly, it appears probable that Meckel's diverticulum can and sometimes does arise from the mesenteric side of the intestine and that the case of Taylor represents the remains of a very small Meckel's diverticulum. Except for this case and the cases of Nicholson, which he believed to be due to inflammation, no cases of gastric mucosa occurring in the small intestines proper could be found.

The stomach, esophagus and whatever remains of the vitelline duct grow relatively slowly as compared with the intestines, which, during the stage when the gastric glands are being differentiated from the primitive endoderm (middle of the second month), are growing so rapidly that they are forced to occupy the celom of the umbilical cord. It seems particularly significant that gastric mucosa has been reported in each of these slow-growing regions of the digestive tract but not in the faster-growing ileum and jejunum. This theory was originally proposed by Stone in 1923, with a statement that the rapid growth of the intestines inhibited the "high degree of differentiation found in gastric mucosa."

Briefly, there are two chief theories in explanation of the occurrence of gastric mucosa in the remains of the vitelline duct:

1. The gastric mucosa represents dislocated fragments of tissue engrafted in the vitelline duct.

2. The simpler and more obvious explanation is that the primitive endoderm, which possesses the pluripotentiality of developing into any one of the several types of epithelium or glands of the digestive tract, is stimulated locally in some undetermined manner to develop into a tissue anomalous for a particular region. Such stimulation has been thought to be irritation, inflammation, lack of bile and relatively retarded growth at certain levels. It appears probable that any or all of these factors may be operative in variable degree.

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THE INJECTION OF EOSIN INTO THE KNEE JOINT

ITS VALUE IN ARTHROSCOPY

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I have previously indicated [1] that eosin tends to stain eroded areas in cartilage selectively; that is, the lesion in the cartilage is stained, but the surrounding normal cartilage is not. I know that this is true of such lesions in tissue examined soon after death. In experimental arthritic lesions produced in the knee joints of rabbits [2] by traumatization of the cartilage of the knee joint with a large bore needle, no selective staining was observed with eosin or with any other dye used. The intensity of staining varies with the concentration of the dye, and the critical concentration at which the synovial membrane stains and the cartilage does not was observed to be a 0.05 per cent aqueous solution of eosin. Since I knew of no other dye with apparent selectivity, I have used only eosin for clinical work.

The pharmacologic behavior of eosin may account for its action on intra-articular injection. It is an acid dye which shows no selective affinity for any particular tissue group by any method of administration, least of all for fat or nerve tissue. Yet a greater receptivity for the dye by damaged or dead tissue cells had been noted, and this was stressed by Rost.[3] Folkmar [4] made this interesting statement: "Just why a living cell is stained by a neutral or basic dye, while a dead cell is stained by an acid dye, is still problematic."

This must be, then, the pharmacologic peculiarity of eosin which makes it selective for diseased areas in cartilage. Yet since eosin is a dye without specific affinity, it may occasionally stain normal cartilage, and in fact it does. But it is observed that the depth of staining of diseased parts is greater than that of any normal part.

From the Hospital for Joint Diseases, the Service of Dr. Leo Mayer.

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Rost and others have adequately demonstrated the absence of toxic effects following the administration of eosin by various routes, and this observation is not denied by my experience with the dye.

I injected from 10 to 20 cc. of a 0.05 per cent aqueous solution of eosin into eleven joints in seven of which the injection was made subsequent to arthroscopy. In a twelfth case a 0.5 per cent aqueous solution of eosin was accidentally injected into the knee joint, and intense diffuse staining of both synovia and cartilage, both of which were normal, was observed through the arthroscope. Visualization of this joint after staining with so strong a solution was poorer than visualization with the unaided eye. Yet no irritation of the joint was noted.

The solution was sterilized before injection, injected in proper amount and immediately reaspirated or flushed out with physiologic solution of sodium chloride or Ringer's solution. Staining was always immediate and superficial The dye caused no irritation whatsoever to the joint and was rapidly absorbed, so that in the two cases in which arthrotomy was done no trace of the dye nor any irritation from it was seen a week later.

It is not necessary to inject eosin into a joint for clear vision at arthroscopy. Yet the dye does make the synovia stand out more clearly, and other structures are better seen. The joint space is stained a fluorescent green, into which a few fine bluish-green synovial villi may be seen floating. The synovia usually stains a light pink, and the villi are clearly outlined against the unusual background of the fluorescent joint space.

It has been my problem to decide definitely whether this dye stains eroded areas in cartilage selectively.

In three cases in which operation was done for the removal of a torn meniscus, the following findings were observed:

In one case it was seen through the arthroscope that the relatively normal femoral cartilage did not stain, although it did have a pinkish tinge. An erosion on the under-surface of the patella was stained deeply. The internal meniscus stained a fluorescent green. At arthrotomy, a week later, no dye was seen in the joint and the surgeon did not examine the under-surface of the patella. In another case, the synovia and the normal cartilage within the joint were stained uniformly. The most interesting case in this group was that of a man of 22 with a tear of the posterior part of the internal meniscus and an erosion of the internal femoral condyle. This eroded area was stained a delicate pink, which clearly delineated it. The joint, which was opened immediately after arthroscopy, showed that this eroded area had stained fairly well but that certain areas in the normal cartilage had stained too. In a youth, aged 17, with osteochondritis dissecans of the external femoral condyle, the normal cartilage had not stained, and the area of dissected cartilage had stained a light pink.

The following findings were noted in six cases of chronic villous synovitis in which the joint cartilage showed little or no change:

In a woman, aged 22, in whom the dye was injected into the joint just before arthrotomy and allowed to remain in the joint for five to ten minutes, there was uniform staining of both cartilage and synovia. In a youth, aged 18, an erosion

on the under-surface of the patella seen through the arthroscope, stained a greenish color, bordered by a ring of red-pink. No note was made regarding the staining of cartilage elsewhere. In a man, aged 27, in whom this disease was localized solely in the synovia, the normal cartilage did not stain; this was also noted in the opened joint. Uniform light staining of the synovia and of the cartilage occurred in a woman, aged 37, in whom synovectomy of the knee had been done more than a year before. A woman, aged 58, in whom arthroscopy alone revealed a villous synovitis and some opacity and fuzziness of the internal femoral condyle showed no staining of the cartilage of the femoral condyles. There was a similar experience in the case of a woman, aged 31, with chronic villous synovitis. The under-surface of the patella did stain a little in streaks. When synovectomy was done on this joint a week later, no dye was seen in the joint. No erosions of the cartilage were seen, and the cartilage in general was a bit more yellowish and fuzzier than is normal.

In the one tuberculous knee, into which the dye was injected preceding fusion of the knee, there was noted a uniform, light pink staining of the synovia, especially of the quadriceps pouch. Several erosions of the femoral condyles had picked up the dye, but several others, which were even larger, had failed to do so. The reason for this was that they were covered by an adherent and inflamed synovia which did not allow contact with the dye. The normal cartilage over the midpart of the femoral condyles did not stain but showed a mild pink.

In none of these cases was an attempt made to determine the p_H of the joint before and after injection or the p_H of the eosin injected. I conferred with Dr. Aaron Bodansky, chemist of the Hospital for Joint Diseases on this particular point. It is not possible to use the indicator method in determining the p_H of the eosinized fluid, and special apparatus is necessary. It is a point worth investigating. Eosin is an acid dye. Any selectivity it may possess should be due to a basic reaction of eroded areas in cartilage.

The reaction of the synovial fluid varies in health and disease. An interesting study by Borghi [5] is pertinent. Using the method of Rous,[6] who had found that certain indicators injected intravitally appeared in the joint fluid, Borghi injected phenol red intravitally in an effort to study the actual reaction of the intra-articular tissues under various conditions, especially the reaction of joint cartilage. Thus, he noted that heat applied to a joint produced alkaline changes; cold applications gave a light and inconstant acidity. Long duration of

5. Borghi, B.: La reazione attuale dei tessuti articolari, Minerva med. **2**: 913, 1930.

6. Rous, P.: The Relative Reaction Within Living Mammalian Tissues: I. General Features of Vital Staining with Litmus, J. Exper. Med. **41**:379, 1925; IV. Indicated Differences in the Reaction of the Organs on Vital Staining with Phthaleins, ibid. **41**:729, 1925.

immobilization produced acid changes, whereas the labor of passive mobilization or of primary motion gave alkaline changes. The changes of disease seldom lower the p_H of the joint fluid lower than 7, according to Seeliger.[7] The protective effect of the oily synovial fluid may retard the staining of the cartilage.

These fundamental theoretical points must be appreciated and completely elucidated before the effects of staining of the joint cartilage by dyes can be fully understood. The paths of absorption of materials injected into joints, especially the knee joint, have been fairly well worked out.

From a practical standpoint, it can be stated, even from this small series of cases, that eosin can cause diffuse staining of normal cartilage and synovia; that, while erosions of various etiology on cartilage will stain selectively with eosin, normal cartilage in the presence of these erosions will also stain, usually in spots. The visualization of an eroded area is made clearer by the use of the dye. Lightly altered cartilage without erosion usually does not stain. Greatly degenerated cartilage stains diffusely.

Since the dye is nonirritating and since it clarifies vision, I see no reason why it should not be used in properly selected cases as an adjunct to arthroscopy.

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7. Seeliger: Ein Beitrag zur pathologischen Physiologie der Gelenke unter Berücksichtigung der Gelenkmausbildung, Arch. f. klin. Chir. **142**:606, 1926.

THERMAL CHANGES IN LOCAL ASPHYXIA AND REACTIVE HYPEREMIA

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It has been known for a little more than fifty years that after local asphyxia there occurs a local vasodilatation, which is nearly a maximal response of the vessels involved provided that the asphyxia has been of sufficiently long duration. The immediate cause of this vasodilatation is unknown. This phenomenon is of frequent occurrence and is of great value to the tissues from a protective standpoint, since it is obvious that in terrestrial life the standing, sitting or lying posture must lead to anemia of the weight-bearing tissues and therefore to a reactive vascular dilatation whenever the static force has been of appreciable duration, perhaps longer than one second.[1] It is obvious that a local anemia is accompanied by increased loss of heat provided that the surrounding climate is cooler than the temperature of the anemic part. This paper is concerned with a quantitative study of the thermal effects in local asphyxia and recovery.

REVIEW OF THE LITERATURE

The term reactive hyperemia was first used by Bier[2] to describe the intense hyperemia of the skin following vascular stasis in the extremity. The most fruitful studies of the problem have been made by the use of various mechanical devices to constrict the blood vessels and observation of: (1) the bright arterial flush in the skin, (2) changes in the volume of the tissues, (3) the rate of inflow of blood following release and (4) changes of systemic blood pressure.

Although it may have been previously observed by physiologists, the first clear description of the phenomenon was made by Cohnheim,[3] who

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1. Goldblatt, H.: Heart **12**:281, 1925.

2. Bier, A.: Virchows Arch. f. path. Anat. **147**:256, 1897.

3. Cohnheim, J.: Untersuchungen über die embolische Processe, Berlin, A. Hirschwald, 1872.

observed flushing after the removal of a ligature applied to the tongue of a frog. Roy and Brown [4] in experiments on the web of the frog's foot observed that there was dilatation of arterioles and capillaries following anemia, that the effect was more marked when the anemia had been of longer duration and that it occurred when the sciatic nerve had been cut. That the hyperemia is of greater magnitude and of longer duration the longer the period of circulatory arrest, within an upper limit, was first observed by Lister [5] and has since been proved by others.[6] Bayliss [7] and others [8] showed that equal periods of occlusion are followed by approximately equal degrees of hyperemia.

Bier [2] showed that reactive hyperemia is a local effect on the tissue occurring independently of the content of blood in the extremity and of the nervous system in man and in the pig. This worker amputated the leg of a pig, except for the femoral vein, and connected the cut ends of the femoral artery with a glass cannula. Obstruction of the flow of blood through the cannula for five minutes was followed by a strong hyperemic flush in the skin. This observation was confirmed by Goldblatt.[1] In the pig Bier excised the dorsolumbar portion of the spinal cord, sectioned both sympathetic chains and then clamped the aorta for five minutes; a strong hyperemia occurred on reestablishment of the circulation. Lewis and Grant [9] showed in man that reactive hyperemia occurred in skin wherein the nerves had degenerated, and this has been confirmed [2] for the dog.

Bayliss [10] found that arterial obstruction in the denervated limb caused a decrease in the volume of the limb and that removal of the obstruction was followed by an increase in the volume of the limb and a fall of general blood pressure. Von Anrep [11] confirmed this observation and showed that if the main artery and vein of the limb were clamped the leg did not decrease in volume but that following release swelling of the limb occurred.

Ingenious experiments devised by Lewis and Grant [12] showed that reactive hyperemia is due to a great dilatation of the involved blood vessels and that it is only slightly less than the changes occurring in

4. Roy, C. S., and Brown, G.: J. Physiol. **2**:323, 1879.

5. Lister, J.: Brit. M. J. **1**:923, 1879.

6. (*a*) Tomita, C.: Arch. f. d. ges. Physiol. **116**:299, 1907. (*b*) Lewis, T., and Grant, R.: Heart **12**:73, 1925. (*c*) Goldblatt.[1] (*d*) Bier.[2]

7. Bayliss, W. M.: J. Physiol. **28**:220, 1902.

8. (*a*) Tomita.[6a] Lewis and Grant.[6b] Goldblatt.[1]

9. Lewis, T., and Grant, R. T.: Heart **12**:209, 1924.

10. Bayliss, W. M.: J. Physiol. **26**:29, 1901; footnote 7.

11. von Anrep, G.: J. Physiol. **45**:318, 1912.

12. Lewis and Grant (footnotes [6b and 9]).

strenuous exercise and somewhat greater than the vasodilatation following exposure to heat. Thus occlusion for ten minutes was followed by greater and more prolonged hyperemia than soaking in water at 44 C. for thirty minutes. Studies of the volume of the limbs suggested that hyperemia occurred in all the tissues. Study of the rate of inflow of blood showed that dilatation occurred during the obstructive phase. These workers also presented strong evidence that the arterioles and capillaries are the chief vessels responsible for the hyperemia. After the removal of a tourniquet the cutaneous hyperemia did not extend as much as 1 mm. beyond the asphyxiated areas. Lewis considered the nature of the vasodilating agent and stated that the effect is probably due to the formation of slowly diffusible metabolites in the extravascular spaces. Bier [13] also concluded that the larger vessels are not involved in the hyperemia. Goldblatt [1] showed that skinning the leg did not abolish this increase of volume of the limb following the release of circulatory arrest.

Krogh [14] presented evidence that lack of oxygen is not the primary factor necessary for the development of the vasodilating substance. He noted by direct observation of the capillaries that completely anemic areas responded to asphyxia by dilatation.

No data are supplied in the present paper concerning the nature of the vasodilating substance. The older work on this subject was reviewed by Fleisch,[15] who stated that an increased acidity is responsible for the increased flow of blood but that doubtless this is not the immediate mechanism responsible for dilating the vessels. The problem is a thorny one. Since normal blood readily acquires vasodilator properties, as was shown by the work of Phemister and Handy,[16] great care is necessary in interpreting data acquired by perfusion methods about such a delicate reaction as reactive hyperemia.

Thermal changes in an extremity in which circulation was arrested were studied by Bazett and McGlone,[17] using the thermocouple method. These workers showed that during stasis there is a definite but very gradual cooling of the tissues, and on release the previous temperature is regained and a still higher level is attained as the result of reactive

13. Bier, A.: Zentralbl. f. Chir. **51**:2, 1924.

14. Krogh, A.: The Anatomy and Physiology of Capillaries, New Haven, Conn., Yale University Press, 1922.

15. Fleisch, A.: Ztschr. f. allg. Physiol. **19**:269, 1921.

16. Phemister, D. B., and Handy, J.: J. Physiol. **64**:155, 1927.

17. Bazett, H. C., and McGlone, B.: Studies in Sensation: Chemical Factor in Stimulation of End-Organ Giving Temperature Sensations, Arch. Neurol. & Psychiat. **28**:71 (July) 1932.

hyperemia. The published data of these workers have been few and do not include a complete thermal record during and after vascular occlusion. Hintze [18] studied thermal effects following the application of a tourniquet by means of a mercury thermometer held in the fingers and concluded that the elevation of the temperature amounted to about 0.5 C. (0.9 F.) above the initial reading and that it persisted for approximately two hours. This worker, as well as many others, showed that cooling of the tissues is not the causative agent of the dilatation.

METHODS

Most of the observations were made on man, although the dog and the rabbit were also used. Unless it is stated that anesthesia was used, the subjects were not anesthetized. All determinations of heat were made with a thermo-electric couple, the component elements of which were copper and constantan. The reference junction was kept in a Sheard constant temperature bath.[19] The variable junctions were of three types. All observations on the skin were obtained with loops of no. 30 gage copper and constantan wire, kept in place on the surface of the skin by a rectangular piece of surgical adhesive tape about 2 by 0.5 cm. The temperature of the muscles was obtained by soldering 44 gage insulated copper and constantan wires into a 26 gage steel hypodermic needle. To obtain the temperature of the bone marrow couples were constructed of 34 gage insulated wires, twisted for about 2 cm. and soldered at the end, which were inserted into the marrow cavity after puncture of the superficial tissue and the bone with a large (18 gage) hypodermic needle. These punctures were made in the rabbit during brief ether anesthesia. A definite lack of resistance was noted when the needle entered the marrow cavity, and blood appeared in the lumen; the couples then entered the marrow cavity to any desired depth, the needle was removed over the wires and the puncture wound was sealed with collodion. The galvanometer [20] was of the D'Arsonval type, with a sensitivity of 0.004 micro-amperes per millimeter at a distance of 1 meter, a period of four and four-tenths seconds, a damping resistance of 280 ohms and a coil resistance of 41 ohms. The thermocouple circuit,[21] including the galvanometer and switches, was composed entirely of copper except for the relatively short section of constantan between the reference and the observation junction. A resistance of 350 ohms in addition to thermocouples, switches, etc., was inserted in the circuit. This gave a deflection of 1.9 cm. per degree centigrade at a distance of 1 meter, and the limit of accuracy of the instrument was 0.05 C. (0.09 F.). The ensemble was repeatedly calibrated against a mercury thermometer, water of known temperature being used in a Dewar flask.

All the experiments were conducted in a quiet, warm (21 to 26 C.) room. Psychrometric determinations of temperature and relative humidity were made. The experimental animals were placed on a table for a preliminary resting period of from ten to ninety minutes preceding all experiments, and throughout the period the table was insulated with blankets to minimize artificial loss of heat.

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18. Hintze, A.: Deutsche Ztschr. f. Chir. **234**:172, 1931.

19. Sheard, C.: Am. J. Clin. Path. **1**:209, 1931.

20. Leeds and Northrop, type R, 2,500 C.

21. Dr. Paul C. Foster, of Tulane University, aided in the design and construction of the circuit.

RESULTS

EXPERIMENT 1.—*Thermal changes in complete asphyxia of limb resulting from mechanical constriction.*

An inflatable cuff of the Riva-Rocci type was placed around the midthigh of a man, and thermocouple loops were placed on the skin over each ankle and knee and above the counter cuff. After a preliminary determination of the temperature the cuff was inflated to a pressure equivalent to 50 mm. of mercury above the systolic blood pressure and maintained for twenty-five minutes. The results in this case, typical of those obtained in twelve determinations in four subjects, are shown in chart 1. In the constricted leg there was a greater fall in temperature of the knee than in that of the ankle; a slow but steady rise of the temperature occurred in the control leg and above the tourniquet in the experimental limb. At

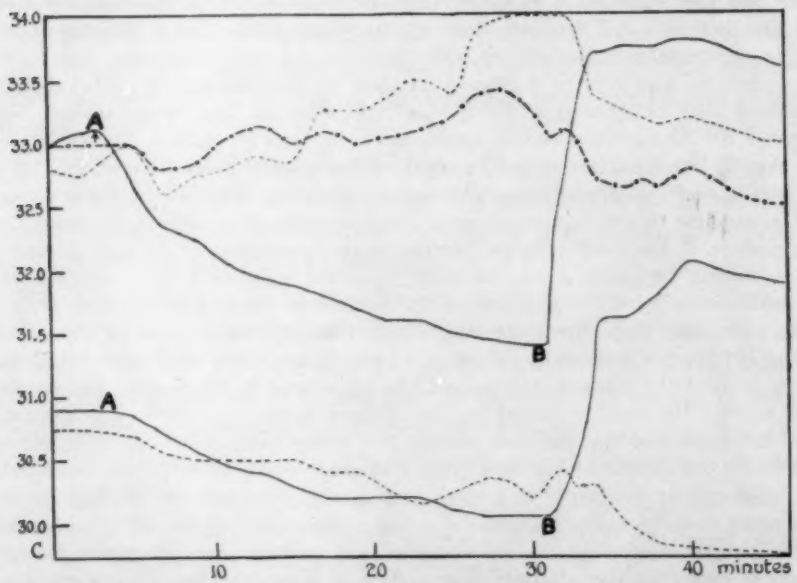

Chart 1 (subject B. H. B.).—A tourniquet was applied for twenty-five minutes on the left midthigh with thermocouples on the skin over the ankle and knee of each leg and above the constrictor on the left leg. The graph shows the lowering of the temperature in the obstructed area with hyperthermia following release. A rise of the temperature in the control areas during the period of obstruction followed by a decrease on the removal of the tourniquet is also shown. The solid lines indicate the changes in temperature at the left medial condyle (upper line) and at the left internal malleolus (lower line). The broken lines indicate the changes in temperature at the right medial condyle (upper line) and at the right internal malleolus (lower line). The broken line with dots indicates the change of temperature on the left thigh above the tourniquet. *A* and *B* indicate the time of application and of removal of the tourniquet.

the time of release, there occurred a large increase in temperature above the initial readings in the constricted leg and a sharp fall in the temperature of the control areas.

Essentially similar results were obtained in six dogs and four rabbits. In these animals an area in the lateral aspect of the upper part of the thigh was infiltrated with procaine hydrochloride, and the anesthetized area was transfixed with a steel pin to hold in position a thin rubber tourniquet used to obtain stasis. Greater thermal changes, both of cooling and of heating, were obtained in these animals than in man, presumably owing to the lesser thermal capacity of the limb. In chart 2 a typical result is shown in a rabbit in which a thermocouple was placed in the marrow cavity of each tibia and in the muscles of the lower hindleg and each foreleg. It will be seen that the increase of heat following circulatory release is much greater in the bone marrow than in the adjacent muscles, and in all experiments the bone marrow was found to heat more than the muscle, the subcutaneous tissue or the skin.

In chart 3 thermal changes are shown in the obstructed leg of a rabbit in which thermocouples were inserted into the marrow cavity of the metatarsal bones, the

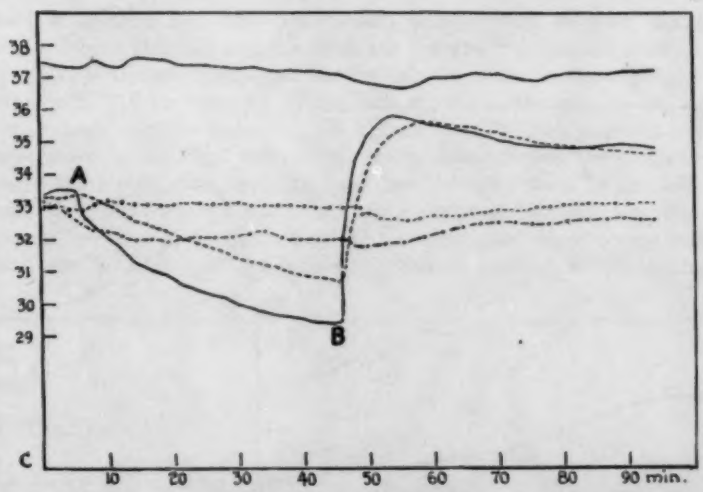

Chart 2 (rabbit 50).—A tourniquet was applied on the left thigh for forty minutes with thermocouples in the muscles and marrow of the lower part of the leg on both sides. The loss of heat during the period of obstruction followed by hyperthermia on release is shown. There was a slight drop in temperature of the control areas on release of the constriction. The solid lines indicate the changes in temperature in the right foreleg intramuscularly (upper line) and in the marrow of the left leg (lower line). The broken line indicates the changes in temperature in the muscle of the left leg. The broken dotted lines indicate the changes of temperature in the muscle of the right leg (upper line) and in the marrow of the right leg (lower line). *A* and *B* indicate the time of application and of removal of the tourniquet.

tibia and the femur. It will be observed that there was no fall of temperature of the cavity of the femur, and a roentgenogram showed that the couple had been inserted above the constrictor. The extent of the thermal changes brought about by stasis and release may be seen.

A series of six experiments were done on human beings. Before the constricting cuff was applied to the thigh, one leg was maintained in an elevated and the

other in a lowered position for five minutes. The cuff was inflated, and the legs were subsequently maintained in a horizontal position. In each instance, as shown in chart 4, there was a greater rise in temperature following release in the leg which had been elevated, and which was pale and relatively anemic, than in the congested leg.

EXPERIMENT 2.—*Thermal changes in the partially asphyxiated limb.*

In the tests on human subjects a Riva-Rocci cuff on the thigh was distended to diastolic pressure and allowed to remain in place for thirty minutes. To obtain an estimate of the amount of blood leaving the leg, 6 mg. of phenolsulfonphthalein (phenol red) was injected into a dorsal vein in the foot immediately after distention of the cuff. The subject voided urine just before the removal of the tourniquet, and the amount of excreted dye was compared with a similar volume of phenolsulfonphthalein excreted under identical conditions without vascular con-

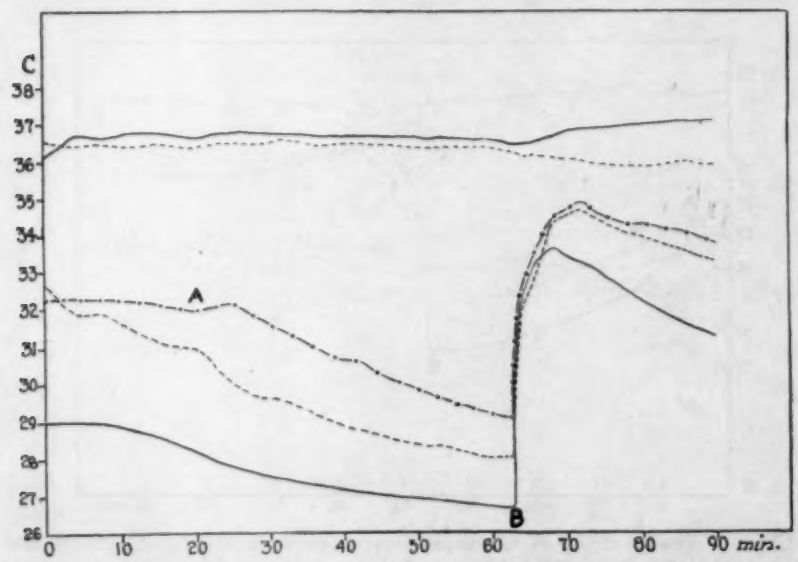

Chart 3 (rabbit 70).—A tourniquet was applied to the right thigh with thermocouples in the marrow of the tibia and the metatarsal bones and in the subcutaneous tissue in the lower part of each leg. The fall in temperature in the control areas and the hyperthermia in the experimental leg on the removal of the obstruction are demonstrated. The solid lines indicate the changes in temperature in the marrow of the right femur above the tourniquet (upper line) and in the marrow of the right metatarsal bones (lower line). The broken lines indicate the changes in temperature in the marrow of the left femur (upper line) and in the marrow of the right tibia (lower line). The broken line with dots indicates the change of temperature in the subcutaneous tissue of the lower part of the right leg. *A* and *B* indicate the time of application and of removal of the tourniquet.

striction. It was found that amounts varying from a trace to 18 per cent of the amount excreted in the control experiment were excreted, showing that the amount of fluid leaving the partially constricted leg is small. As is shown in chart 5, the temperature fell slightly in the congested leg and continued to fall after the removal

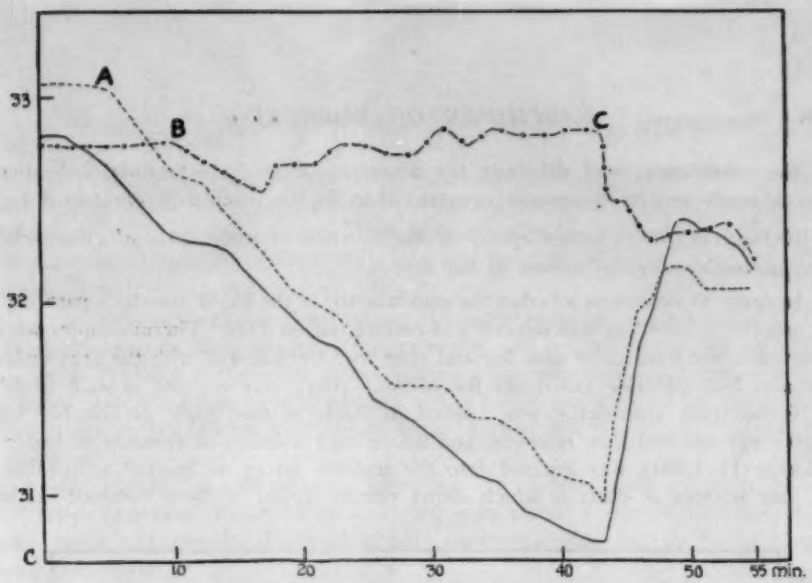

Chart 4 (subject M. O.).—Tourniquets were applied to both legs after the left leg had been elevated and the right leg lowered for five minutes. A greater degree of hyperthermia developed in the left leg than in the right. A fall of temperature of 0.5 C. occurred in the skin of the upper part of the right arm after the release of the circulation. The broken line with dots indicates the changes in temperature in the right arm. The broken line indicates the changes of temperature of the right foot, and the solid line indicates those in the left foot. *A* indicates the time at which the left foot was elevated and the left foot was lowered. *B* indicates the time of application of the tourniquet and of returning both legs to the horizontal position, and *C* indicates the time of removal of the tourniquets.

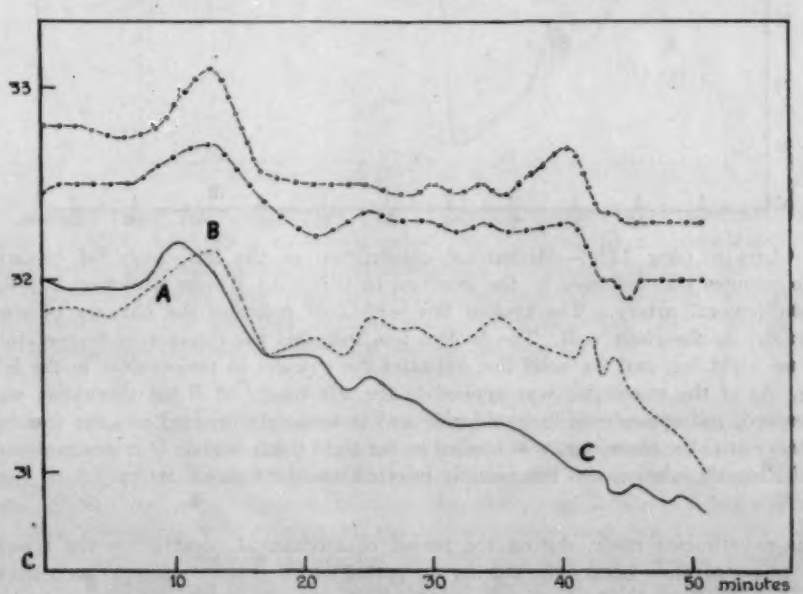

Chart 5 (subject C. H.).—Application of mechanical stasis at diastolic pressure (70 mm. of mercury) on the left leg for thirty-one minutes was not followed by hyperthermia in the leg. The broken lines with dots indicate the changes in temperature in the left knee (upper line) and in the right knee (lower line). The broken line indicates the changes in temperature in the right foot, and the solid line indicates those in the left foot. At *A* the tourniquet was applied to the right thigh; at *B* phenolsulphonphthalein was injected into the right leg, and at *C* the patient voided urine, and the tourniquet was removed.

of the constriction, and this was not accompanied by hyperthermia, indicating that a much smaller hyperemia occurred than in the completely obstructed leg.

EXPERIMENT 3.—*Thermal effects of the injection of large doses of epinephrine into the main artery of a limb of the dog.*

In order to determine whether the musculature of the blood vessels is paralyzed or not, this experiment was devised and carried out on dogs. Thermocouples were inserted in the muscles of each leg and over the sternum, and with the area under procaine hydrochloride anesthesia the femoral artery was exposed in each groin. A rubber tube constrictor was applied as high in the thigh as possible for twenty minutes and then removed, and 0.5 cc. of a solution of epinephrine hydrochloride (1:1,000) was injected into the femoral artery as quickly as possible. As may be seen in chart 6, which shows results typical of those obtained in the

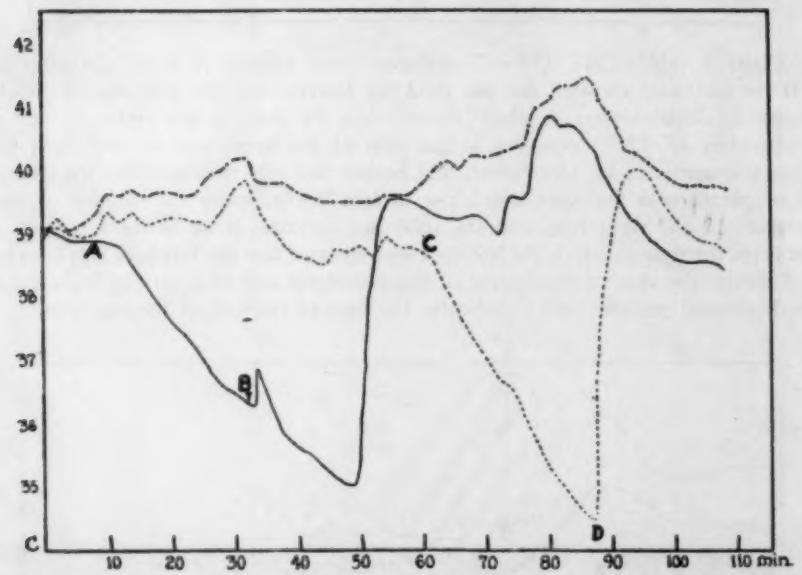

Chart 6 (dog 132).—Mechanical constriction of the left thigh for twenty-two minutes was followed by the injection of 0.5 cc. of Ringer's solution into the right femoral artery. The broken line with dots indicates the changes of temperature in the chest wall. The broken line indicates the changes of temperature in the right leg, and the solid line indicates the changes in temperature in the left leg. At *A* the tourniquet was applied to the left thigh; at *B* the tourniquet was removed, and epinephrine hydrochloride was immediately injected into the femoral artery; at *C* the tourniquet was applied to the right thigh, and at *D* it was removed, and Ringer's solution was immediately injected into the femoral artery.

four experiments made, during the period of mechanical constriction the typical fall of temperature occurred. During the period of injection of epinephrine a slight rise occurred, obviously due to warm blood entering the leg, but this was quickly followed by a further lowering of the temperature at the same rate as with mechanical constriction for eighteen minutes, when a temperature above the initial readings occurred. In order to evaluate the effect of mechanical inter-

ference with the circulation due to the needling of a main artery, a tourniquet was then applied on the control leg for twenty minutes, and after its removal, 0.5 cc. of a 0.9 per cent solution of sodium chloride was injected into the lumen of the control femoral artery. This did not interfere with the development of typical local hyperthermia.

In another series of five dogs, 0.5 cc. of a solution of epinephrine hydrochloride (1:1,000) was injected into the femoral artery. A typical thermal curve is seen in chart 7; there occurred a steady fall of temperature in this animal for one hundred minutes, followed by a gradual rise of temperature to normal, but without hyperthermia. A rise in temperature above normal did not occur in any animal of this series.

Since the fall in temperature following the experimental injection of epinephrine resembled closely that following mechanical constriction, observations were made to determine how complete the vasoconstriction was in the latter case.

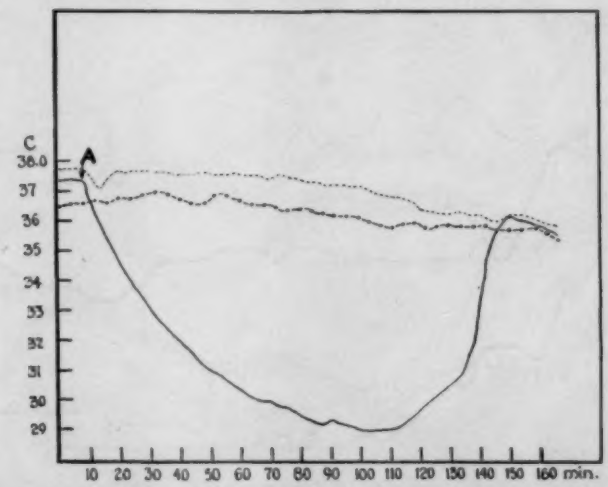

Chart 7 (dog 907).—Injection of 0.5 cc. of epinephrine hydrochloride solution (1:1,000) into the left femoral artery was followed by a gradual lowering of the temperature and then by hyperthermia. The broken line indicates the changes of temperature in the right leg; the broken line with dots indicates those in the chest wall, and the solid line indicates those in the left leg. At *A*, 0.5 cc. of epinephrine was injected into the left femoral artery.

In four dogs weighing between 8 and 16 Kg., under ether anesthesia, a cannula was inserted in a carotid artery to obtain a record of blood pressure, and an injection of 0.5 cc. of epinephrine hydrochloride (1:1,000) into the femoral artery was made. A typical experiment in a dog weighing 9 Kg. follows. Three minutes subsequent to the injection, the leg was amputated just below the knee joint, without any mechanical attempt to control hemorrhage, and a vessel was held below the site of operation to collect any blood lost. Three drops of blood (0.3 cc.) was lost during the procedure. The amputated portion was pale and appeared grossly to be almost completely bloodless. For two hours the stump of the leg was allowed to lie open and unsupported over the collecting vessel. There occurred a very slight ooze of blood and during this time, in all, 2 cc. of

blood came from the wound. The vessels became occluded with blood clots, so that after the constricting effects of the epinephrine had worn off there was no bleeding. At the end of this two hour period the normal leg was amputated at the same site without hemostasis and without injection of epinephrine; the dog died in sixteen minutes of anemia, having lost 293 cc. of blood. This evidence is rendered as proof that injection into the femoral artery of relatively large amounts of epinephrine causes complete vasoconstriction and renders the tissue supplied by the artery essentially bloodless.

EXPERIMENT 4.—*Thermal effects of injection of large doses of epinephrine into the main artery of a limb in man.*

In three men a relatively large dose (0.5 to 0.75 cc.) of epinephrine hydrochloride (1:1,000) was injected into the femoral artery just below the inguinal

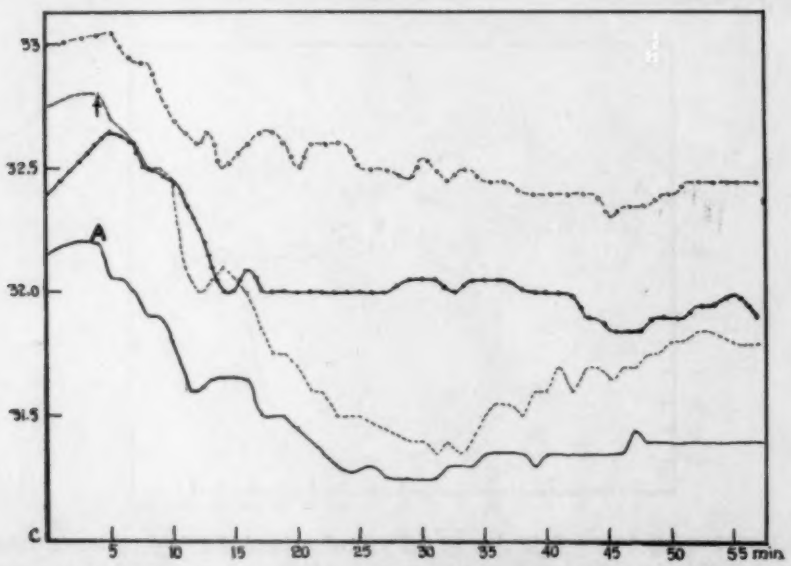

Chart 8 (subject M. O.).—Cutaneous temperature readings over both ankles and knees after the injection of epinephrine hydrochloride solution into the right femoral artery. Reading from the top down the lines indicate the changes in temperature in the left medial condyle, the left internal malleolus, the right medial condyle and the right internal malleolus. At *A*, 0.75 cc. of epinephrine hydrochloride (1:1,000) was injected into the right femoral artery.

ligament. In subject M. O. (chart 8) there was a rise in the systemic blood pressure of 68 mm. of mercury in four minutes, accompanied by tachycardia and slight dyspnea. The experimental leg became cadaveric in its waxy-white appearance, and there was complete obliteration of the pulses in the dorsalis pedis and posterior tibial arteries. There were few unpleasant sensations in the anemic leg, and cooling occurred. The recovery began in about twenty-five minutes after the injection; there developed in the skin a circumferential band of hyperemic flush about 15 cm. in length which appeared first in the midthigh and progressed in a bandlike fashion to the foot. As the hyperemic band progressed centrifugally,

involving new skin, the proximal hyperemic area faded, and when it reached the lower part of the leg, the arteries of the foot began to pulsate weakly and soon returned to normal. The process of recovery was associated with a mild tingling in the foot, much less than that experienced following the removal of a tourniquet.

In subject F. N. a 28 gage needle was inserted into the lumen of the femoral artery, blood was withdrawn and 0.75 cc. of epinephrine hydrochloride (1: 1,000) was injected. Apparently the injection was made directly into the wall of the artery, because after the injection blood could not be aspirated in the syringe, and there occurred at the site of injection a pronounced systolic thrill and a loud harsh bruit, both of which persisted for one hour, then diminished and were completely absent in two hours. There were no symptoms of absorption of epinephrine as in the preceding subject.

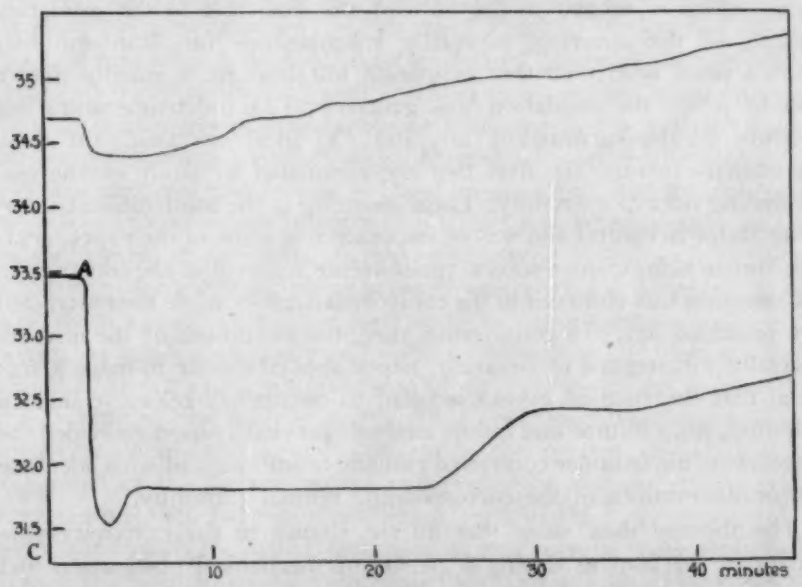

Chart 9 (subject C. H.).—Result of the injection of 0.5 cc. of epinephrine hydrochloride into the subcutaneous tissue of the lateral part of the right thigh adjacent to the thermocouple with a similar injection of Ringer's solution into the left thigh at the same time. The time of injection is indicated at *A* on the chart. The upper line indicates the changes in temperature in the left thigh, and the lower line indicates those in the right thigh.

EXPERIMENT 5.—*Local injection of epinephrine into the subcutaneous tissues.*

Observations were made on three men in the following way: A thermocouple needle was inserted in the subcutaneous region of the lateral part of both thighs. After control readings of temperature were made a hypodermic needle was inserted and 0.5 cc. of epinephrine hydrochloride (1: 1,000) was injected in such a way that the thermocouple point lay in the approximate center of the wheal produced. Into the opposite thigh 0.5 cc. of Ringer's solution was injected. In each case the fluid injected was warmed to about 32 C. In each case the infiltration was accompanied by a fall in temperature, much greater and of longer duration in the case of epinephrine (chart 9).

COMMENT

It is obvious that circulatory changes can be profitably studied in the limb from a thermal standpoint provided a lower temperature exists in the laboratory than in the area studied. When the extremity the circulation of which was obstructed was kept at body temperature, there was no loss of heat. Since a very small amount of heat is produced in a quiet extremity, an increase of heat must mean an increased flow of blood from the interior of the body, and a rise of temperature in the quiet extremity therefore indicates an increased flow of blood. Cooling need not mean a decreased flow of blood, but it must be interpreted in the light of the following factors: (1) the thermal capacity of the tissue, which is related to the bulk of the limb and to the insulating capacity of the covering, especially subcutaneous fat, skin and hair (thus a small limb with thin insulation lost heat more rapidly than a limb in which the insulation was greater); (2) the temperature and moisture of the surrounding air, and (3) local sweating. Of these adventitious factors, the first two are eliminated by study of the corresponding normal extremity. Local sweating is the most difficult interfering factor to control and was of importance in some of the experiments with human beings, since several times before removal of the constricting cuff sweating was observed in the control extremities while the obstructed limb remained dry. In considering, then, the limitations of the method, especially with regard to sweating, which applied chiefly to man, it was found that the thermal events incident to circulatory release coincided with flush, limb volume and inflow methods previously used, provided the studies were made under controlled climatic conditions and with adequate control observations of the corresponding normal extremity.

The thermal data show that all the tissues in the extremity participate in the cooling during a period of mechanical obstruction and in the hyperthermia following release. It seems proved that hyperemia occurs in bone marrow and in muscle as well as in the skin; it may be seen from charts 2 and 3 that there was no lag in the increase of heat in the deep tissues, such as would be anticipated were the hyperemia confined to the skin, with conduction of heat producing elevation of the temperature of the deeper structures.

It was found that greater increments of heat occurred in the deeper tissues, especially in the bone marrow, than in the skin. This is at least partially accounted for by increased insulation of the deeper tissues, with less chance for loss of heat than in the skin.

The recovery from mechanical obstruction of circulation in the limb was in each case followed by hyperthermia when the duration of the arrest had been longer than fifteen minutes. In sharp contrast, in

no case in which the circulatory arrest was produced by injection of epinephrine alone was recovery associated with hyperthermia, although this was associated with a hyperemic flush of the skin. However, in experiments in which mechanical arrest was immediately followed by constriction with epinephrine, not only was the period of constriction produced by epinephrine much shorter than that in the cases in which intra-arterial injection was not preceded by the application of a tourniquet, but a hyperemic hyperthermia resulted. Apparently a vasodilating substance produced by mechanical obstruction of the blood flow shortened the effect of the epinephrine.

The fact that injections of epinephrine into large arteries of the limb produce vasoconstriction in the areas supplied agrees well with observations of previous workers.[22] Falta and Priestley[22c] found that large doses of epinephrine injected into the femoral artery of dogs frequently produced no elevation of systemic blood pressure, and they concluded that large amounts of this substance remained in the extremity under these circumstances. Hess,[22b] the only previous worker who used human subjects, reported that no rise in blood pressure followed this procedure, as opposed to the results reported by Elliott and other workers on dogs. In the present experiments, as opposed to those of Falta and Priestley, a rise in general systolic blood pressure was always observed in man as well as in animals; the dose used in these experiments was, however, somewhat larger than that used by Hess. Phemister and Handy[16] found that the injection of small quantities of epinephrine caused a decrease in the volume of the limb in dogs. That the vasoconstriction following intra-arterial injections was complete in the present observations was suggested by the thermal curves and proved by the amputation experiments, which showed that constriction, even of the large arteries of the limb, occurred. It was of interest that recovery in these experiments was slow enough that sufficient coagulation of the blood took place on the surface of the cut extremity to prevent hemorrhage after the vasospasm had disappeared. The hyperemic flush occurring in recovery, in which a circumferential band of hyperemia formed in the thigh and moved centrifugally toward the foot while the proximal areas faded, indicates that spasm disappeared first in the proximal vessels and recovery occurred centrifugally. This is perhaps the explanation of the fact that a hyperthermic hyperemia did not occur following the intra-arterial injection of epinephrine; enough blood vessels were not dilated at any one time to produce an elevation of temperature. The fall in temperature caused by the local injection of epinephrine into the tissues

22. (*a*) Elliott, T. R.: J. Physiol. **32**:401, 1905. (*b*) Hess, O.: Arch. f. exper. Path. u. Pharmakol. **91**:303, 1921. (*c*) Falta, W., and Priestley, J. G.: Berl. klin. Wchnschr. **48**:2102, 1911.

agrees with much previous work [23] which has indicated continued spasm of local blood vessels.

The fall of temperature in the control areas when a mechanical tourniquet was removed from another limb has not been previously observed. This decrement, amounting to from 0.3 to 3 C. (0.5 to 5.4 F.), always occurred. It is undoubtedly related to the fall in systemic blood pressure and perhaps indicates vasoconstriction. It is not entirely due to the passage of blood through a cool limb. In a series of five experiments on man, mechanical arrest of circulation was produced in both legs with an inflated cuff while thermal changes in the arm were measured. At the time of arrest of circulation the obstructed limbs were covered with blankets and heated with electric lights, so that a great increase in local heat occurred (to 40 C. [72 F.]). When the tourniquets were removed, a slight fall in the temperature of the arm alway occurred.

Lewis and Grant [6b] concluded that after an increase of venous pressure a state of vasodilatation occurs of very similar grade to that produced by arterial occlusion. In none of the present experiments was the hyperemia of sufficient degree to produce hyperthermia, which always occurred after comparable periods of arterial obstruction by mechanical means.

CONCLUSIONS

The thermal changes following circulatory obstruction and release are comparable to those produced by the previous methods of studying these phenomena, provided certain limiting factors in the method are controlled. Mechanical obstruction results in decrement of heat, and release is followed by a hyperthermia in the limb.

Chemical obstruction of the circulation by intra-arterial injections of epinephrine is followed by a similar decrement of heat but differs from stasis produced by mechanical means in that hyperthermia does not occur after release. A preceding mechanical arrest of circulation shortens the effect of an immediately subsequent intra-arterial injection of epinephrine and leads to hyperthermia.

Injections of epinephrine hydrochloride into the femoral artery of the dog and of man in doses of 0.5 to 0.75 cc. (1:1,000) produce complete vascular spasm even of the large arteries, and recovery as judged by the visual observation of hyperemic flush of the skin occurred in a centrifugal manner, beginning proximally in the thigh. Not only do the thermal curves noted after the injection of epinephrine suggest complete arrest, but amputation below the knee was accompanied by very slight hemorrhage.

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23. Rous, P., and Drury, D. R.: J. Exper. Med. **49**:435, 1929.

Greater increments of heat occur in reactive hyperemia in the bone marrow than in the muscle of the skin in the extremity and in the limb rendered anemic before occlusion than in the congested limb.

After release of constriction in the extremity there occurs a fall in the temperature of the unobstructed limbs.

A method for determining the temperature of the bone marrow is presented.

A REVIEW OF UROLOGIC SURGERY

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KIDNEY

Tumors.—Wharton [1] contended that the outlook in the treatment of malignant tumors of the kidney is improving because of the use of radiation preoperatively to reduce the size and make nephrectomy feasible and because of the transperitoneal approach for removal.

The results of lumbar nephrectomy for renal tumor have been poor because these growths, which reach enormous size, are highly vascular, are made up of friable tissue which is characteristically transplantable and have a thin, delicate capsule which is easily ruptured. The mobilization and manipulation necessary before the renal pedicle can be reached and ligated tend to produce hemorrhage, distant metastasis from milking tumor cells into the blood stream and local recurrences from rupture of the capsule. The last structure to be seen and controlled is the renal pedicle, whereas it should be the first.

These disadvantages of lumbar nephrectomy are eliminated by the transperitoneal approach, which permits one to see the tumor clearly, to expose and ligate the renal vessels before it is handled or moved, to ligate aberrant vessels and the collateral venous supply, which is usually enormously enlarged, and to remove intact the kidney with the surrounding tissues, the capsule of Gerota, the perirenal fat and areolar tissue and as much of the ureter as is desired. Since these advantages

† Deceased.

1. Wharton, L. R.: Transperitoneal Nephrectomy for Malignant Tumors of the Kidney, Surg., Gynec. & Obst. **60**:689 (March) 1935.

of transperitoneal nephrectomy are obvious, the chief reason that it has not been universally adopted is probably because of its technical difficulties and the unfamiliarity of urologists with the upper part of the abdomen.

Wharton described a simple and safe operation which obviates these difficulties. Preliminary treatment, consisting of diet, rest, the administration of tonics, the control of hematuria and irradiation, is given for three or four weeks. At operation the patient is placed in the dorsal position with the back hyperextended. A long rectus incision is made, and the intestines are packed into the opposite half of the abdomen. The posterior peritoneum is incised 2.5 cm. from the lateral margin of the large bowel, mobilized, and cut well above the flexure of the large intestine; it is then pushed away from the region of the renal pedicle and kidney, carrying with it the colon and the duodenum on the right side. Before the renal vessels are clamped, they should be thoroughly exposed by removal of the fat and areolar tissue by which they are concealed. After their division, aberrant vessels and the collateral venous supply are controlled, and the tumor, ureter and all of the perirenal tissue possible are removed intact. The posterior portion of the peritoneum is closed by a continuous, plain gut suture. Drainage is established by an extraperitoneal stab wound in the flank.

Priestley and Broders [2] reviewed 65 cases of Wilms' tumor at the Mayo Clinic. In 20 cases nephrectomy was performed, the remaining patients being treated symptomatically or by irradiation. Early symptoms are usually lacking. The method of choice in treating these patients is preoperative irradiation, followed in from three to six weeks by nephrectomy and by extensive postoperative irradiation. Of 44 patients traced up to the present time, 40 are known to be dead. No patient treated by irradiation alone is known to be living. Of the 20 patients who underwent nephrectomy, 15 are dead, 4 are living and 1 was not traced. Of the 4 patients who survived nephrectomy, only 2 have survived for any appreciable length of time (thirteen and two-tenths years and three and two-tenths years, respectively). The other 2 patients were operated on only six months ago, too recently to permit any conclusion regarding the final result.

Karácson [3] reported 2 cases of primary epithelial tumor of the pelvis of the kidneys and ureters. In 1 case, that of a 50 year old woman, a positive preoperative diagnosis could not be made. On surgical

2. Priestley, J. T., and Broders, A. C.: Wilms' Tumor, J. Urol. **33**:544 (June) 1935.

3. Karácson, A. V.: Ueber die primären, epithelialen Geschwülste des Nierenbeckens und des Harnleiters, auf Grund von 2 Fällen, Ztschr. f. urol. Chir. **40**:205, 1934.

exploration the kidney and ureter appeared to be normal, and the condition was diagnosed only on examination of the specimen. Karácson expressed the belief that total nephrectomy is necessary in order to prevent recurrence. The second case was that of a man, aged 69, who had hematuria for two weeks. The ureterogram revealed in the pelvic part of the ureter a filling defect typical of tumor of the ureter. Nephrectomy was performed, following which the patient recovered. Karácson called attention to the necessity of determining the condition of the remaining stump of the ureter in order to be certain that no further tumorous growth remained.

Stone.—Brown [4] stated that in 1891 von Recklinghausen described certain skeletal changes, namely, marked softening of bone with deformity and multiple sarcomas, which he designated as osteitis fibrosa. In 1925 Mandl and Uebelhör resected a tumor of the parathyroid gland in a case of generalized osteitis fibrosa and observed the general and skeletal improvement that occurred. Since that time numerous observers have contributed to the knowledge of this condition. A case of hyperparathyroidism in which the symptoms were those of renal lithiasis was reported from the Mayo Clinic by Brown.

The normal excretion of calcium in the urine varies from 0.1 Gm. per day in persons on a diet low in calcium to 0.5 Gm. per day in those on a normal diet. Hunter and Aub and Johnson and Wilder also found that on the administration of parathyroid hormone the amount of calcium excreted in the urine was increased markedly. It is known that whatever the varying causes of the formation of stone in the urinary tract, the one definite factor is abnormal precipitation of crystalline elements normally present in the urine. Obstruction and infection may be causative factors, but probably, as has been demonstrated experimentally by Keyser, a marked increase in the normal urinary crystalloids adds so much to the burden put on the protective colloids that they are unable to perform their work efficiently, and precipitation is likely to occur. With an increased content of calcium in the tissues and in the blood stream, such as exists in cases of hyperparathyroidism, there is a marked increase of the amount of calcium in the urine, and precipitation with formation of calculi is likely to occur.

Attention has repeatedly been called to the association of hyperparathyroidism and nephrolithiasis. Castleman and Mallory observed the presence of renal stone in 20 of 25 cases of hyperparathyroidism reported from the Massachusetts General Hospital. In 11, the presenting symptoms were referable to the urinary tract, and the skeletal changes were minute or were overshadowed by the renal lesions.

4. Brown, A. E.: Hyperparathyroidism with Nephrolithiasis, Proc. Staff Meet., Mayo Clin. **10**:417 (July 3)1935.

Albright stated that renal calculi may occur in cases of hyperparathyroidism without lesions of bone and that the former may be an index of the severity of the disease and the latter an index of the duration of the disease. The importance of performing routine tests for the determination of the calcium and phosphorus content of the serum in cases of nephrolithiasis is emphasized.

Camp,[5] in discussing Brown's case, stated that the roentgenologic findings are interesting because they serve to emphasize the incidence of nephrolithiasis in cases of hyperparathyroidism and the assistance the roentgenologist may be in arriving at the diagnosis. The roentgenologic changes in the skeletal system in the moderately advanced stages are well established and characteristic, and the average roentgenologist should have little difficulty in making the diagnosis. However, in the early stage, in which there is a minimum of osteoporosis and in which the bones have not yet acquired the characteristic granular appearance, the diagnosis is difficult. Because of this fact the presence of generalized osteoporosis, regardless of its degree, plus associated nephrolithiasis, should lead to the exclusion of the presence of hyperparathyroidism.

Barney and Mintz [6] report their experience with hyperparathyroidism in relation to the formation of urinary stones. One hundred and four patients with urinary calculi were examined, a complete examination of the blood being made to determine the calcium and phosphorus content. A diagnosis of hyperparathyroidism was made in 18 of the cases. Of these, 11, or 61.1 per cent, presented not only tumor of the parathyroid gland but also urinary calculi. This makes a percentage of 10.5 persons with calculi associated with hyperparathyroidism in the group of 104 patients. The 11 patients, all having stones, together with 7 others without stones but with cystic degeneration of the bones, have all been operated on, and an adenoma of the parathyroid gland was removed. Twelve of the patients were females and 6 were males, and the ages varied from 13 to 62 years. The calcium content of the blood varied from 11.5 to 16.8 mg. per hundred cubic centimeters, and the phosphorus content, from 1.4 to 4.7 mg. Barney and Mintz stated that a calcium content of the serum above 11 mg. per hundred cubic centimeters and a phosphorus content below 3.5 mg. should always arouse suspicion of a disease of the parathyroid gland in association with renal calculi.

Albright and Bloomberg [7] stated that hyperparathyroidism is a sufficiently frequent cause of the formation of renal stone that its presence

5. Camp, J. D., in discussion on Brown.[4]

6. Barney, J. D., and Mintz, E. R.: Some Newer Conceptions of Urinary Stone Formation, J. A. M. A. **103**:741 (Sept. 8) 1934.

7. Albright, Fuller, and Bloomberg, Esther: Hyperparathyroidism and Renal Disease, J. Urol. **34**:1 (July) 1935.

must be considered in every case of the disease. Eleven cases are cited from a series of 23 proved cases of hyperparathyroidism at the Massachusetts General Hospital in which the presence of renal stones was the only indication of the underlying disease. A frequent finding in cases of hyperparathyroidism is the presence of many finely granular casts in the urinary sediment. The granules have been shown to contain calcium, probably calcium phosphate. The casts can be made to change into hyaline casts as the urine is made more acid by the administration of ammonium chloride by mouth. Their continuous presence in large numbers is an indication that intrarenal damage is occurring. Probably the factors governing the formation of these casts, which might be designated as microscopic calculi in the renal tubules, are the same that govern formation of stone in cases of hyperparathyroidism. These factors are the concentrations in the urine of calcium, phosphate and hydrogen ions. The formation of stone in cases of hyperparathyroidism belongs to the group wherein the predisposing abnormal factor is an excess of crystalloids in the urine.

According to Herman and Lee,[8] greater familiarity with the clinical picture and the biochemical problems of cystine urolithiasis has accounted for an increasing number of case reports. Cystinuria, which has an incidence of about 1 : 500, is predominantly a disorder of males (from 70 to 80 per cent) and is inheritable. Because of faulty metabolism of protein leading to incomplete oxidation of sulfur, cystine, a sulfur-bearing amino-acid, appears in the urine in excessive amounts, usually in solution but occasionally in crystalline form. When the usual accessory factors of urolithiasis, infection or obstruction are present, cystine stones are likely to form. Clinically they have a tendency to occur at an earlier age than other stones, and they are multiple and have a tendency to recur rapidly and to vary in radiopacity. At times, large numbers of fairly large stones may be passed with ease because of their waxy texture.

Although the same principles that apply to the treatment of urolithiasis in general hold good for cystine stones, a more conservative attitude toward operative treatment may be adopted because: (1) larger cystine stones will pass more readily than other varieties of stones, (2) there is in the absence of, and according to some writers in spite of, proper postoperative treatment, a marked tendency to rapid recurrence, and (3) in certain instances cystine stones may be dissolved by alkalis, internally and locally.

In cases of cystinuria attempts should be made to prevent the formation of stone by alkalization, which maintains the solubility of cystine

8. Herman, Leon, and Lee, W. E.: Cystine Nephrolithiasis, Ann. Surg. **101**: 746 (Feb.) 1935.

in the urine. Limitation of proteins, especially of those rich in sulfur, is a rational phase of prophylactic treatment.

Congenital Urinary Anomalies.—Wiseman [9] pointed out the dangers lurking in the urinary pathway occasioned by the presence of a congenital anomaly, which may prove to be the source of obstruction and consequent urinary stasis and infection and the necessity for prompt relief in cases of such obstruction. The cases discussed exemplify the predominance of gastro-intestinal manifestations in the syndrome of obstruction of the urinary tract, in some instances to the exclusion of disturbances in the urinary tract; in other cases the gross findings in the urinary tract are normal. The applicability of plastic procedures for the relief of obstruction and the provision for drainage of hydronephrotic sacs have been offered as the most appropriate surgical attack, thereby preserving renal integrity, whenever the diagnosis has been made before the parenchyma is irreparably damaged.

Tuberculosis.—Chwalla [10] discussed spontaneous healing of renal tuberculosis. He first gave a critical survey of the few cases of spontaneous healing of chronic renal tuberculosis that have ever been reported in the literature. He established the fact that in most of these cases there was not a real cure in the sense of scarring over of the affected area, with retention of renal function; in most of the reported cases cure was only apparent.

Chwalla reported a case which he believed was an instance of true spontaneous healing of unilateral renal tuberculosis. The patient was a 20 year old girl whose history showed a tuberculous condition. There were many typical tuberculous ulcers and granulations in the bladder, being most numerous in the region of the orifice of the left ureter, which was red and edematous. There was decreased function of the left kidney, and the urine from this side was turbid. It was impossible to catheterize the left ureter because of an impassable obstruction 1.5 cm. above the orifice. Mycobacterium tuberculosis was found in the urine from the bladder. The right kidney was normal. At operation the left kidney was apparently not abnormal and was left in place. Two and a quarter years later the urine from the bladder was clear and free from bacilli; the return of indigo carmine was normal from both sides. Eight and ten years later, cystoscopy and inoculation of animals showed no evidence of tuberculosis. Chwalla based his assumptions on the fact that the existence of primary tuberculosis of the bladder has so far not been proved, and nothing in his case pointed to genital tuberculosis.

9. Wiseman, J. L.: Congenital Urinary Anomalies, Ann. Surg. **100**:445 (Sept.) 1934.

10. Chwalla, Rudolf: Gibt es eine Spontanheilung der Nierentuberkulose? Wien. klin. Wchnschr. **47**:882 (July 13) 1934.

Greenberger, Wershub and Auerbach [11] attempted correlation of the incidence of renal tuberculosis in a careful study of 500 cases of pulmonary and extrapulmonary tuberculosis. Of the 500 cases in which routine necropsy was done, 252 gave evidence of tuberculous infection of the kidney. Miliary tubercles were found at 228, or 45.6 per cent, of all necropsies. These small tubercles appeared grossly as gray or yellow, single or conglomerate, the lesions often lying in rows and following the medullary rays into the renal pyramids. Microscopic examination of the sections revealed that they varied from necrotic areas to fibrotic tubercles. Tuberculous involvement of the kidneys was bilateral in 187 cases, or 82 per cent. The youngest patient was 9 months old; the oldest, 74 years; 157 were males and 71, females; 154 were of the white, 72 of the Negro and 2 of the yellow race. Only 25 per cent had urinary symptoms. The most common complaints were nocturia and frequency of urination. Destruction of the renal substance was found at necropsy in only 24 of the 500 cases, or 4.8 per cent. These statistics indicate the high incidence of renal tuberculosis secondary to advanced pulmonary tuberculosis in a large municipal sanatorium. The nondestructive, closed or miliary tuberculous lesion in the kidney was most common; the destructive, open or chronic surgical tuberculosis of the kidney is notably deficient in symptoms despite advanced renal involvement.

According to Eisendrath,[12] the association of renal tuberculosis and true calculous formation occurs in approximately 1.8 per cent of all cases of renal tuberculosis. Although the total number of cases is comparatively small, the possibility of such an association should be constantly borne in mind. Eisendrath reviewed 35 cases reported in the literature since 1920 and added 5 of his own. In the first place distinction must be made between the calcification which occurs in about 7 per cent of all cases of renal tuberculosis and true calculous formation. The former has definite roentgenologic characteristics, which have been described by Crenshaw. Eisendrath divided the cases of true calculi into 4 clinical groups. In the majority (26 of the 40 cases) there were stone and tuberculosis on the same side. A correct diagnosis was made in only 1 of the reported cases in this group. In the majority the stone was evident, but the tuberculosis was unsuspected. Nephrectomy is indicated. If the presence of tuberculosis is unsuspected and a less radical operation is performed, there is likely to be a persistent postoperative fistula and an early recurrence of stone.

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11. Greenberger, M. E.; Wershub, L. P., and Auerbach, Oscar: The Incidence of Renal Tuberculosis, J. A. M. A. **104**:726 (March 2) 1935.

12. Eisendrath, D. N.: Renal Tuberculosis and Nephrolithiasis as Associated Diseases, Surg., Gynec. & Obst. **60**:777 (Jan.) 1935.

There were 5 patients with tuberculosis on one side and stone on the other. All of them, at intervals varying from one month to one year following nephrectomy for tuberculosis, had anuria from the stone in the remaining kidney or ureter. Therefore, in a case of unilateral tuberculosis the opposite side should be examined carefully for stone. If a stone is present, it should be removed either by operative or by nonoperative methods before nephrectomy is carried out.

There were 4 patients with bilateral renal or ureteral calculi and unilateral tuberculosis. Eisendrath advised removal of the stone in the nontuberculous kidney before nephrectomy is performed on the opposite side. There are two other groups: those with bilateral renal tuberculosis and unilateral nephrolithiasis and those with bilateral renal tuberculosis and bilateral nephrolithiasis. They are of interest from the diagnostic standpoint. The treatment is that of bilateral renal tuberculosis.

Cystic Disease.—Geisinger [13] discussed the nature, characteristics, clinical picture and treatment of renal cystic disease. A series of 8 cases were reported. There were 5 cases of polycystic disease, in 1 of which nephrectomy was required, and 2 cases of solitary cysts, 1 being an instance of the rare bilateral type. There was also 1 case of arteriosclerotic kidneys, with cystic degeneration in each of a type suggesting a further clinical demonstration of the operation of the Hepler theory of the origin of so-called solitary cyst of the kidney.

URETERAL TRANSPLANTATION

Hinman [14] reviewed his results in 37 cases of uretero-intestinal implantation and called attention to his modification of Coffey's technic 3. He employed the latter in 3 cases, with unsatisfactory results.

There are renewed efforts at present to improve the technic of uretero-intestinal implantation so as to prevent infection and ureteral obstruction. These efforts are directed largely to bilateral simultaneous implantation for use in adults with acquired lesions, chiefly vesical carcinoma, in whom added surgical procedures multiply the risk. Coffey's technic 2 (bilateral drainage by means of a catheter) has proved unsatisfactory because of dangers of ureteritis and suppurative nephritis from the catheters—disadvantages which were recognized by Coffey. Higgins' modification of Coffey's technic 3 and Poth's modification of Higgins' technic have the advantage of asepsis and free drainage of urine into the bladder until the anastomosis is established. However,

13. Geisinger, J. F.: The Cystic Kidney, J. Urol. **34**:202 (Sept.) 1935.

14. Hinman, Frank: Uretero-Intestinal Implantation with Drainage by Extraperitoneal Catheter, Surg., Gynec. & Obst. **60**:1115 (June) 1935.

the difficulty of fixing both uncut ureters into the bowel without tension, which may result in detachment later, is a decided disadvantage.

In 7 cases, in 6 of which there was a single kidney, Hinman performed nephrostomy preliminary to implantation. The 6 patients with single kidneys, all of whom had intractable tuberculous cystitis, recovered. Nephrostomy was indicated in these cases of tuberculosis as a therapeutic measure in itself. After the patients improved, it was possible to determine the feasibility of uretero-intestinal implantation. However, drainage by preliminary nephrostomy should not be regarded as a stage of uretero-intestinal implantation. It complicates the problem by increasing the surgical risk, but it has its own indications.

Experience with extraperitoneal drainage after ureterotomy led Hinman to express the opinion that it might be used in conjunction with Coffey's technic 3 (transfixion-suture method), thus permitting bilateral simultaneous implantation. In the original technic only one ureter can be transplanted at a time. The ureter is exposed, opened and drained by a ureteral catheter extraperitoneally above the site of the anastomosis. This method was used in 3 cases. The result was satisfactory in the first case, in which the patient had the ureter of a single kidney transplanted to relieve an intractable tuberculous cystitis, but was unsatisfactory in the other 2 cases. The method is not recommended.

Sherman, Dinardo and Bowers [15] presented a new technic for simultaneous bilateral transplantation of the ureters into the rectosigmoid. A pure metallic magnesium tube is used to aid in canalization and to prevent both early and late obstruction at the site of implantation. The magnesium tube undergoes a chemical change in the presence of acid urine and slowly dissolves; it therefore requires no further attention. The results obtained in experiments on animals have been satisfactory The immediate results obtained in man appear to warrant further use of this method.

Cabot [16] stated that during the past fifteen years much attention has been given to various methods of diverting the urine, all of which present some difficulty. There are three methods available at the present: nephrostomy, uretero-enterostomy and cutaneous ureterostomy.

Nephrostomy may be used as an intermediate step for drainage of the kidney when temporary diversion is indicated in cases in which rearrangement of damaged ureters is to be carried out. Cabot expressed the belief that it is rarely the best method for permanent diversion, since it is not notably more certain to preserve the integrity of the kidney and is more inconvenient than cutaneous ureterostomy. The

15. Sherman, W. L.; Dinardo, C. J., and Bowers, J. M.: Ureteral Transplant: Preliminary Report of a New Technique, Am. J. Surg. **29**:54 (July) 1935.

16. Cabot, Hugh: Diversion of Urine Above Level of Bladder, Surg., Gynec. & Obst. **61**:406 (Sept.) 1935.

cases suitable for uretero-enterostomy are almost always those in which the ureters are substantially normal; the attempt to transplant abnormal ureters is likely to be followed by a higher mortality and by less satisfactory results. It is most useful in cases of congenital anomaly, certain injuries of the bladder and in a few cases of chronic interstitial cystitis. It may be employed as a preliminary to total cystectomy for cancer, but the mortality will be higher, since both ureters must be moved at the same time, and it is desirable to perform cystectomy either at the same sitting or after a brief interval. It must not be assumed on the basis of the present evidence that uretero-enterostomy enables the upper part of the urinary tract to remain entirely normal for an indefinite period; some degree of dilatation associated with infection is the rule. For patients with grossly abnormal ureters, and when the bladder has ceased to be useful, cutaneous ureterostomy has been shown to produce a lower mortality and a relatively satisfactory result. If the operation is technically well performed, and particularly if a catheter of fair size is kept permanently in the ureter up to the level of the renal pelvis, the patient is dry and comfortable and can live an effective life.

PROSTATE GLAND

Hypertrophy.—Willing[17] discussed the treatment for prostatic hypertrophy. Between 1912 and 1932, 625 patients with hypertrophy of the prostate gland were treated in the surgical clinic at Göttingen University. Two hundred and fifty-nine patients were treated without surgical intervention, and 22 per cent of these died; suprapubic prostatectomy was performed on 288 patients, and 16 per cent died following the operation. Perineal prostatectomy was done on 13 patients, with a mortality of 23 per cent; cystostomy was performed on 65, with a mortality of 37 per cent.

Pitrolffy-Szabó[18] reported the results of a study of the histologic changes in cases of hypertrophy of the prostate gland. He sectioned and examined 32 prostate glands removed surgically. Arteriosclerosis was found in 72.2 per cent and inflammatory conditions in 91 per cent. He did not consider either of these findings of etiologic importance. Basal cell metaplasia occurred in 18.2 per cent, and malignant changes occurred in 12 per cent of the cases.

Page[19] outlined Fullerton's method of prostatectomy and reported the results in 31 cases. Prior to operation the value for blood urea and

17. Willing, Waldemar: Ueber die Behandlung der Prostatahypertrophie, Beitr. z. klin. Chir. **159**:576, 1934.

18. Pitrolffy-Szabó, Béla: Beiträge zur Histologie der Prostatahypertrophie: LXII. Wissenschaftliche Sitzung der Ungarischen urologischen Gesellschaft anlässlich der Ungarischen Arztewoche, Ztschr. f. urol. Chir. **40**:210, 1934.

19. Page, W. A.: Prostatectomy as Performed by the Late Professor Andrew Fullerton, Brit. M. J. **1**:578 (March 23) 1935.

Calvert's range of urea concentration were ascertained. A urea content of less than 50 mg. per hundred cubic centimeters was essential. If it exceeded 50 mg., operation was postponed until the patient's condition improved. When the results of these preliminary investigations were unsatisfactory, an indwelling catheter was inserted.

In only 1 of the 31 cases was a two stage operation performed, and this was done because of the patient's intolerance to an indwelling catheter. The fibrosis produced by the use of a suprapubic catheter interferes with the speed and simplicity of the major operation and the healing of the second wound. The anesthetic used in all these cases was a mixture of chloroform and ether, followed by ether given by the open drop method. Inhalation anesthetics were considered safe over such a short period as was necessary for the operation, and any risk attached to their use was not any more than that of the shock which in rare cases attended the employment of spinal anesthetics in their other operations.

The aim of the operation was speed. While the patient was being anesthetized, all possible preparations were made so that he would not be on the table more than fifteen minutes. The prostate gland was enucleated in the usual way. The hemostatic bag was inserted and distended, and a large rubber drainage tube was slipped over the abdominal end of the hemostatic bag into the bladder. The wound was then closed. No attempt was made to remove tags or to secure bleeding points in the prostatic cavity. Owing to the fact that the mortality increased in an earlier series of cases in which these methods were used, the operation was discarded. Ligation of the vas deferens was not favored, since it was considered better to allow any infection to travel to the epididymis, where it did no particular harm, than to be dammed back by a ligature and start a never ending vesiculitis. The hemostatic bag used was Fullerton's modification of the Pilcher bag. It was rounded, to avoid the possibility of incontinence occurring as a result of the apex of the Pilcher bag being pulled down through the sphincter urethrae and stretching that muscle beyond the limits of recovery.

The postoperative treatment was simple. The hemostatic bag and drainage tube were left in place for forty-eight hours. The bottom of the bed was raised on blocks, and pressure was maintained on the prostatic cavity by attaching a weight of 2 pounds (0.9 Kg.) to a thread which came from the interior of the bag down the urethral tube. The weight was then hung over the end of the bed. The patient usually had an uncomfortable feeling that the bladder required to be emptied while the bag was in situ, but the hemostasis obtained was excellent. At the end of twenty-four hours the fluid was removed from the bag, and

the bed was lowered to the horizontal position. Forty-eight hours after operation the bag and drainage tube were removed.

There was 1 death in the 31 cases in which the patient was operated on by this method. Epididymo-orchitis occurred in 5 cases. With suitable treatment this cleared up in from four to seven days. Periurethral abscess was observed in 2 cases. Fistulas developed, but in both instances the fistula healed before the patients left the hospital. They were treated by suture over a catheter, after the edges of the fistula were cleaned.

Prostatic Resection.—Caulk and Harris [20] stated that in using the various high frequency cutting instruments for resection of the prostate gland deeper damage to tissue is frequently produced than is desired and that to some extent it is unavoidable. High current densities applied for more than a second may do damage at depths from a few millimeters to more than a centimeter. In order that tissue may be cut with high frequency currents, an intense heat is required at the active electrode. To produce this heat it is necessary for the current to pass through the tissue from an indifferent electrode and to focalize at this point. In so doing, the paths of the current, in their concentration toward the active electrode, generate varying degrees of temperature deep within the tissue, away from the point of active burning, whereas in removal with the actual cautery approximately the same temperature is applied at the surface of the cut but no heat is produced within the tissue except by conduction from the surface.

Smith and Stockwell [21] stated that clinical observation and pathologic study indicated that chronic prostatitis, which obtains in the majority of cases of obstruction of this gland, with attendant edema of the gland and adjacent structures of the neck of the bladder, is the underlying factor in these cases in which necrosis, sloughing and infection develop to a dangerous degree. In comparison with prostatectomy, when the element of renal or cardiac insufficiency is significant in the evaluation of mortality or morbidity risk, the hazard of resection of the prostate gland is usually confined to localized physiopathologic changes in the prostatic region.

Preliminary dehydration or shrinking of the prostate gland has been used by Smith and Stockwell in 125 cases. It reduced the morbidity, and there were no deaths in the series. Dehydration is per-

20. Caulk, J. R., and Harris, Wilbur: A Study of Comparative Effects of Various High Frequency Currents and of Thermal Cauterization in Prostatic Resection, J. Urol. **32**:449 (Nov.) 1934.

21. Smith, C. K., and Stockwell, A. L.: Preliminary Shrinkage of the Prostate in Transurethral Resection, Together with Histological Study of the Action of the Coagulating and Cutting Currents, J. Urol. **34**:31 (July) 1935.

formed under light spinal anesthesia; several lines of lightly applied coagulation, with the use of the Stern-McCarthy resectoscope and the McCarthy roller electrode, are run over the gland in a parallel direction from the neck of the bladder forward to the region of the verumontanum. The intention is not to destroy tissue but to establish a mild reactionary inflammatory process. The lines are run at intervals, complete sealing off of the prostatic surface being avoided and allowance being made for drainage of infectious and inflammatory products. When active infection is present, suprapubic drainage is first established by a tube introduced through a large caliber trocar. In certain instances a severe infection is allowed sufficient time to correct itself before any instrumentation is attempted. An advantage attending preliminary shrinkage is that with the edematous element eliminated a clean, concise molding of the outlet of the bladder can better be accomplished.

Hambleton, Lackey and Van Duzen [22] made an investigation to determine whether the evolution of an explosive gas usually accompanies the use of high frequency currents in transurethral resection of the prostate gland; and, if so, at what rate the gas was evolved, its composition and how the danger of explosion might be minimized. In experiments on a series of 12 dogs there was produced in each instance a gaseous mixture which was not explosive in the absence of oxygen from external sources but became so on the addition of the proper proportion of oxygen or air. When such mixtures were exposed directly to the arc from the resection apparatus they exploded inside the bladder. The violence of the explosion was sufficient to give a loud report when it took place in the exposed bladder, but in the healthy bladders of the dogs used no ruptures were produced.

The rapid rate at which highly inflammable gases may be evolved during the use of high frequency currents for transurethral resection emphasizes the necessity of caution in order to prevent the occurrence of serious accidents. Since a small volume of gas mixed with air is sufficient to produce a violent explosion, simple lavage after each series of cuts cannot be considered an adequate safeguard unless the entrance of air is rigidly prevented. The diverse character of the gases in the mixture precludes the possibility of their removal by an absorbent. If a large amount of air or gas collects in the bladder, as shown by a large bubble, this should be aspirated by inserting a ureteral catheter into the bubble, before cutting or coagulation is done. When the patient is placed in the Trendelenburg position, the bubble is brought closer

22. Hambleton, B. F.; Lackey, R. W., and Van Duzen, R. E.: Explosive Gases Formed During Electrotransurethral Resections, J. A. M. A. **105**:645 (Aug. 31) 1935.

to the area to be coagulated and the danger of explosion is increased, as explosion does not occur unless the arc comes in direct contact with the gas.

BLADDER

Tumors.—O'Crowley [23] reported that in 902 cases of carcinoma of the bladder recorded in the Carcinoma Registry of the Urological Association, 436 growths were papillary carcinomas, 446 infiltrating carcinomas and 20 carcinomas of an unusual type. Of the 866 carcinomas that were graded, 20 per cent were of grade 1, 33 per cent of grade 2, 35 per cent of grade 3 and 12 per cent of grade 4.

The location of 854 of these tumors of the bladder, involving adjacent or multiple areas, was as follows: trigon, 32.2 per cent; lateral walls, 35.3 per cent; neck of the bladder, 9 per cent; posterior wall, 10.2 per cent; vault, 7.5 per cent, and anterior wall, 5.7 per cent. In only 473 of these cases was one area of the bladder alone involved, which was as follows: trigon, 27.37 per cent; lateral walls, 41.89 per cent; neck of the bladder, 5.89 per cent; posterior wall, 10.92 per cent; vault, 7.58 per cent, and anterior wall, 6.32 per cent. Ten per cent of the cases in the Registry which were studied at necropsy showed metastasis in the following order of frequency: bones, lungs, regional lymph nodes, liver and retroperitoneal lymph nodes. Wound implantations were rare; there were none reported in this series of 902 cases. Regardless of the grade of the tumor, the percentage of recurrence varied little and followed initial treatment in 46.2 per cent of cases. Multiple tumors are more likely to recur than single growths, which is probably due to the growth of new tumors. This suggests that new growth of the bladder is possibly a diffuse disease of the mucosa or possibly results from a general circulating cancerogenic substance.

The size of the tumor bears a definite relationship to the prognosis. Of 48 patients with tumors ranging from 1.9 to 2.4 cm. in diameter, 54.2 per cent were alive at the end of five years. Of 91 patients with medium-sized tumors, between 2.4 and 4.9 cm. in diameter, 39 per cent were alive at the end of five years; whereas of 155 with tumors larger than 5 cm., 25 per cent were alive at the end of five years. As to the mortality in the cases in the Registry according to the different grades of malignancy, at the end of five years there was a mortality of 33 per cent among 71 patients with tumors of grade 1. Among 82 with tumors of grade 2, the mortality was 60 per cent for the five year period; among 120 with tumors of grade 3, 80 per cent, and among 42 with tumors of grade 4, 95.5 per cent. In this series only 102 patients are living more than five years following operation.

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23. O'Crowley, C. R.: Carcinoma of the Bladder, Arn. Surg. **101**:1407 (June) 1935.

In the whole group the most unsatisfactory results seem to have been obtained by resection or excision with a scalpel. The total estimated mortality in all cases in which patients were so treated was 85 per cent, as compared to a general mortality of 66 per cent. Excision or resection cannot be the operation of choice, owing to the inaccessibility of many tumors. Fulguration by the actual cautery has advantages over resection but is not so effective as cold cautery plus the radio knife. According to these statistics a combination of fulguration and excision in 287 cases carried a mortality of 52 per cent in three years, as compared to a general mortality of 66 per cent. The results in these cases were, however, much more favorable than those in which radium was used. In many instances the condition had progressed too far for fulguration, and radium was implanted. It was concluded that for the general run of carcinomas of the bladder seen by the urologist a three year cure can be expected in nearly half of the cases by this method, which is more effective than resection.

Beer [24] grouped growths of the bladder into three clinical and pathologic classes: benign papillomas, papillary carcinomas and solid infiltrating carcinomas, often of the squamous cell type. Further subdivision, based on microscopic data, only leads to confusion, as does the interpretation of infiltrating characteristics by the pathologist and the surgeon. A tumor may be superficial and reveal infiltration of the stalk or of the pedicle. Such a growth can be approached with some success by electrocoagulation or radium. In the infiltrating group are included growths that invade the wall of the bladder. They can frequently be felt by rectum or vagina before operation and feel, after thorough extraperitonealization of the organ, like a solid, more or less nodular plaque in the wall of the bladder. In the literature both groups appear as infiltrating; for the former, results from any form of treatment are fair; for the latter, no treatment but wide resection or total cystectomy will give satisfactory results. Seeding with radium or coagulating the really solid, infiltrating growths is a hit-or-miss procedure. Further confusion occurs in the interpretation of results by designating benign papillomas as "group 1 carcinomas" and reporting as infiltrating carcinomas those in which the involvement is superficial.

Some papillomas recur locally or in different regions after complete, well controlled destruction. In other cases papillary carcinomas or even solid growths develop years after destruction of the original growth or growths. In some cases after excision or control of solid carcinomas there are benign recurrences, although too frequently they are malignant; these are not truly recurrences but are overlooked or left-in parts of the original tumor.

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24. Beer, Edwin: Surgery of Bladder Tumors, Ann. Surg. **101**:1412 (June) 1935.

Beer was of the opinion that if adequate materials are available, one should be equipped to apply all types of therapeutic methods in cases of tumors of the bladder. He was fairly certain of only two things: Benign papillomas can be destroyed and cured transurethrally or suprapubically with the high frequency current, and papillary carcinomas, infiltrating the wall of the bladder deeply, and solid infiltrating carcinomas can be completely and regularly removed only by total cystectomy. Partial cystectomy, the more extensive the better, and usually with the sacrifice of the ureter and neostomy, gives a fair result (40 per cent in three years) in cases of infiltrating papillary carcinoma, whereas the solid infiltrating growths are a more difficult problem, although partial cystectomy has resulted in cures. Radium has been used extensively in both these groups with a higher mortality than that following partial cystectomy; cure results only occasionally in cases of deeply infiltrating growths, and then only after considerable prolonged suffering.

During recent years many methods of approach have been developed in the treatment of tumors of the bladder. The approach in these cases cannot be limited to any one method; a great variety of methods should be available for use, depending on one's own experiences and on that of others. The following procedures are available: transurethral electrocoagulation with the bipolar or monopolar current; transurethral introduction of radon seeds; high voltage roentgen therapy; suprapubic cystotomy with electrocoagulation of the tumor and its base, or with electrocoagulation or excision combined with implantation of radon seeds; suprapubic, extraperitoneal resection of the involved wall of the bladder, with transplantation of the ureter or with ligation of the ureter; various combinations of the foregoing procedures for multiple tumors; resection of the main tumor and electrocoagulation or radium implantation for secondary or small tumors, and suprapubic, total cystectomy and partial prostatectomy for infiltrating malignant growths at the neck of the bladder, with transplantation of the ureters into the skin of the iliac region or with transplantation of the ureters into the colon.

Barringer [25] stated that the grading of tumors has been a significant aid in making a comparison of different methods of treatment possible. According to Broders' system, tumors of the bladder have been graded into four classes: grade 1, corresponding to a papilloma, and grades 2, 3 and 4, indicating increasing degrees of malignancy. Radium probably is not indicated in the treatment of papillomas; fulguration through the cystoscope or through a cystotomy wound is probably the best treatment. Extensive papilloma of the entire wall of the bladder is most

25. Barringer, B. S.: Radium Treatment of Cancer of the Bladder, Ann. Surg. **101**:1425 (June) 1935.

satisfactorily treated by cauterization through the open bladder after the method of Beer. It is Barringer's belief that tumors of grade 2 are real cancers. As far as the grade of malignancy is concerned, tumors of grade 2 and 3 can be treated either by surgical methods or by radium. Treatment of tumors of grade 4 either by radium or by surgical measures is probably inefficient; only 1 patient was cured by radium.

Tumors of the base or lateral walls of the bladder coming in proximity to the ureters or internal urethra occurred in 61 per cent of the 78 cases; in 32 per cent of the cases the tumor was on the lateral wall at the base of the bladder, back of the trigon or in the vault, and in 6 per cent the location was not given. In 165 cases from the Mayo Clinic these statistics were practically reversed, 66 per cent of the tumors occurring on the lateral walls and in the vault, and 33 per cent in the base of the bladder, trigon, urethra or orifices of the ureters. Tumors of the base are treated easily by radon seeds implanted either through the cystoscope or through the cystotomy wound. Tumors of the apex are as well treated by radium as by surgical methods, and possibly more satisfactorily by the latter method. Tumors of a diverticulum are satisfactorily treated surgically by removal of the tumor and the diverticulum. If there is secondary involvement of the bladder, radium may supplement surgical treatment. Tumors of the bladder secondary to tumors of the prostate gland are preferably treated by radon seeds implanted through the open bladder. Tumors protruding from the orifice of the ureter and secondary to tumors of the ureter are treated by surgical measures alone. If there is a secondary involvement of the bladder, implantation of radon seeds may supplement surgical treatment.

With increase in the size of the base of the tumor, radium takes ascendancy over surgical treatment, until there arrives a time when the latter is totally ineffective and radium is reasonably effective. In 78 controlled cases the base of the tumor in 21 cases (27 per cent) was between 1 and 4 sq. cm.; in 16 cases (20 per cent), between 4 and 6 sq. cm., and in 37 cases (47 per cent), more than 6 sq. cm. In 17 of the 37 cases the base was 20 sq. cm. and involved half or more than half of the bladder. In 4 cases the area of the base was not given. Large bulky tumors of the top of the bladder, even if they involve the ureters, are preferably treated by surgical measures.

In the first series of 109 cases there were 4 deaths in the hospital, a mortality of 3.6 per cent. In 179 cases there were 13 deaths (7.2 per cent) in the hospital. In 134 of Dean's cases in which radon seeds were implanted there were 9 deaths (6.7 per cent) in the hospital. Of 205 of Barringer's own cases 66 (32 per cent) were controlled; 50

(24.3 per cent) of the patients were well after three years and 44 (21.4 per cent) after five years.

Implants of radon seeds are peculiarly applicable in controlling tumors of the bladder, but this is not true of the radium element in needles. There is almost always a single plane, about 1 cm. deep, to irradiate, and needles are too awkward and large to irradiate such a plane effectively. Radium needles, moreover, have to be removed, while radon seeds do not, and there is a possibility that radium needles will be displaced during the process of the treatment.

Dean [26] stated that the average successful dose of radiation for treating tumors of the bladder is about from 7 to 10 skin erythema doses within sixteen days. The 4 Gm. radium pack is not suitable for treating this lesion because of the time required to administer a satisfactory dose. The 200 kilovolt unit can furnish about 50 per cent of the required dose. Therefore, it offers slight hope of curing a tumor of the bladder, and even its palliative value is questionable. The 700 kilovolt unit can so closely approximate the required dosage that one is justified in employing it in the treatment of cancer of the bladder. It is assumed that a complete urologic examination has been made in all cases and that the choice of treatment has been made by the urologist.

Counseller and Braasch [27] stated that the use of diathermy in the surgical management of carcinoma of the bladder is gradually being extended, for it has brought cases in which the condition formerly would have been regarded as inoperable, or the growth as nonresectable, within the field of successful treatment. Seventeen patients whose conditions were considered inoperable were treated extensively with diathermy alone, and 15 of the 17 (88 per cent) lived more than five years. Two others have recently died from unrelated conditions. Tumors of the bladder that are comparatively small and are of a malignancy of grade 1 or 2 are usually controlled by transurethral electrocoagulation. Some of the early, circumscribed lesions which are graded 3 or 4 and which can be seen easily and give no clinical evidence of infiltration may be treated similarly. The more extensive, highly malignant lesions and the widespread lesions with low degrees of malignancy are attacked preferably by the suprapubic route. Whenever the lesion can be completely removed surgically, by either segmental resection or excision, this is the operation of choice. Electrocoagulation is used for the inoperable lesions, of both high and low grades of malignancy, confined to the base. The small number of recurrences and the lack

26. Dean, A. L., Jr.: Treatment of Bladder Cancer with External Irradiation, Ann. Surg. **101**:1428 (June) 1935.

27. Counseller, V. S., and Braasch, W. F.: Diathermy for Carcinoma of the Bladder, Ann. Surg. **101**:1418 (June) 1935.

of deformity and infection of the bladder would recommend this method of treatment. In some instances these procedures may be combined with the application of radon seeds or of needles containing radium. The advantages of diathermy as a transvesical procedure for inoperable or nonresectable lesions of both high and low grades of malignancy have not been sufficiently recognized.

Quinby [28] stated that it is unfortunate that malignant neoplasms of the urinary bladder show a marked tendency to be situated in the base of the organ. In a recent study of 902 cases of tumors of the bladder in the Registry for Carcinoma of the Bladder, more than 75 per cent of the growths were found to originate on the trigon, on the neck of the bladder or low on the lateral wall. This means that less than a quarter of all carcinomas of the bladder are accessible to surgical removal without interference with the ureteral insertion or the vesical sphincter.

The operative removal of the urinary bladder inevitably includes the problem of diversion of the urine. There are three possible methods of disposal of the urine after the bladder has been removed: It may be delivered directly to the loin through a nephrostomy or a pyelostomy wound; each ureter may be brought out onto the abdominal wall in the inguinal or lateral regions, or the ureters may be implanted into the intestine. The disadvantage of each of the first two methods is the early and serious infection of the kidneys, besides the necessity of some sort of apparatus to collect the urine with all the attendant discomfort and complicated care. The dangers of uretero-intestinal anastomosis are the risk of immediate operative infection resulting in peritonitis and later renal involvement from obstruction to the flow of urine away from the kidney or infection or both.

At the urologic clinic of the Peter Bent Brigham Hospital it has seemed advisable not to apply one single form of treatment to cancers of the bladder but so far as possible to treat the disease in each instance by excision or radium or by partial or complete cystectomy, as seems most applicable and likely to give the best results. In those cases in which total cystectomy has been performed operability by this method has been judged on the basis of four criteria: 1. The carcinoma not only must be found to be situated in the base of the bladder but must be in such close proximity to the vesical sphincter that removal by any method must result in incontinence. 2. There should be no demonstrable metastasis of the tumor to the regional lymph nodes or to those at the aortic bifurcation. Cystectomy has not been performed in any case in which preliminary laparotomy has shown such extravesical pro-

28. Quinby, W. C.: Total Cystectomy for Cancer of the Bladder, Ann. Surg. **101**:1415 (June) 1935.

gression of the malignancy. 3. Renal function must be normal in at least one kidney, but preferably in both, as demonstrated by ureteral catheter. 4. Actively growing carcinoma must be demonstrated on microscopic examination.

All patients are first studied by cystoscopy and by roentgenologic examination of the chest and skeleton to exclude a diagnosis of metastasis. Renal function is estimated, and pyelograms are made; retrograde pyelograms are made if possible, and if not, intravenous ones. At the first operation the region of lymphatic drainage away from the bladder is investigated, and if no secondary deposits of malignant tissue can be determined, anastomosis of a single ureter is performed. Following recovery from this operation, the second ureter is transplanted, and the bladder, together with the prostate gland of the male, or of the whole urethra of the female, is excised. The electrosurgical needle is of advantage in the conduct of the anastomoses as well as in the excision of the bladder. Ten patients to date have been treated in this manner. Two are alive; one is a woman who for three years has been without evident recurrence, and the other is a man who in the eight years following treatment has had recurrence about the rectum and prostate gland during the past year. Of the remaining 8 patients, 2 died as a direct result of an early form of the operation, which was imperfect in some way. The remaining 6 have died of recurrent cancer at longer or shorter periods after operation. In none of these cases, however, was there any further acute difficulty in the urinary tract.

Nesbit [29] stated that cystectomy for malignant growths of the bladder is indicated in cases in which there is such involvement of the trigon that the orifices of the ureters cannot be spared when destructive methods of treatment are used, in cases of infiltrative involvement of the outlet of the bladder so that adequate attack locally is destructive to the sphincters, in cases of multiple infiltrative tumors and in cases in which the neoplasms are of a low grade of malignancy but have a marked tendency to recur and spread in spite of conservative treatment and eventually become penetrative or highly malignant.

There are three methods of disposing of the urine following cystectomy. Drainage of the kidney by nephrostomy or pyelostomy has disadvantages that contraindicate its use if other methods can be utilized. Cutaneous ureterostomy has long been considered a safer method than uretero-intestinal anastomosis. The drainage tubes and apparatus necessary following the latter procedure are difficult to manage and can rarely be fitted sufficiently well to prevent some leakage of urine. The

29. Nesbit, R. M.: Total Cystectomy and Ureteral Transplantations in Malignant Conditions of the Bladder with a Description of a New Operative Procedure, J. A. M. A. **105**:852 (Sept. 14) 1935.

most satisfactory method from the standpoint of functional results is uretero-enterostomy. Coffey's technic 1 is probably the safest of the three methods described by him, since transplantation is carried out in two stages, cystectomy requiring a third operation. The prolonged period of hospitalization is a disadvantage. Coffey's technic 2, in which bilateral simultaneous transplantation with ureteral catheters is done, was used in 9 cases. Three of the patients died before leaving the hospital.

In an effort to eliminate the high mortality of ureteral transplantation, a less hazardous procedure has been sought. A two stage method has been developed and has been employed recently in 2 cases of malignant disease of the bladder. At the first stage both ureters are mobilized for a distance of 10 cm., at about the level of the pelvic brim, and are embedded between the muscularis and the mucosa of the upper part of the rectum without opening the lumen of the intestine or interrupting the continuity of the ureter. Healing of this area takes place by primary union. The second stage is done from fourteen to twenty-one days following the first stage. The ureters are severed 2.5 cm. distal to the area of implantation. A purse-string suture is then laid in the wall of the intestine about the base of the severed ureter. A small incision, extending into the lumen of the intestine, is made as closely as possible to the base of the stump of the ureter. The end of the ureter is introduced into the lumen of the bowel and the purse-string drawn, completing the anastomosis. Advantages of this method have been demonstrated experimentally. There is no interruption of urinary flow at any time. Primary union of the areas of first stage implantation prevents the constriction which is so commonly seen following direct implantation. Ascending infections in the wall of the ureter have been noticeably absent in experimental animals.

Caulk [30] stated that disturbances of the physiologic activities of the kidneys and ureters occur in a large proportion of cases of malignant tumor of the bladder and contribute at least 50 per cent to the mortality. Early diagnosis and prompt treatment of a tumor of the bladder afford the most satisfactory protection against such involvement. The tendency of the majority of these growths to be situated near the trigon, their pronounced inclination to invade and the likelihood of their causing secondary infection make the fate of the upper part of the urinary tract precarious. Safeguarding the ureter is essential in the treatment of a tumor of the bladder; every precaution should be used to protect it from trauma. It has been Caulk's experience that the safest and most satisfactory procedure in the treatment of this lesion of the bladder is

30. Caulk, J. R.: The Upper Urinary Tract in Carcinoma of the Bladder, Ann. Surg. **101**:1432 (June) 1935.

the application of radon seeds and coagulation, either suprapubically or, preferably, endovesically. Occasionally an erosive destructive tumor which implicates the ureter requires resection with reimplantation. In many cases such a tumor may be satisfactorily treated by intravesical implantation, the orifices of the ureters being guarded by an indwelling catheter. Reimplantation of the ureter in the hands of the average surgeon is fatal to the kidney. In cases of generalized carcinomatous change throughout the vesical cavity, actual cauterization, with or without the implantation of radon seeds, occasionally yields satisfactory results. Total cystectomy has a limited field; when performed, it demands preliminary ureteral drainage, preferably through an iliac-cutaneous implant, and rarely preliminary uretero-intestinal anastomosis. Ureterostomy or nephrostomy is occasionally necessary as a palliative measure to relieve suffering and to prolong life.

Diverticulum.—Melen [31] discussed the various surgical procedures for treating diverticula of the bladder and described a lateral approach through a pararectus or modified Gibson incision. This facilitates exposure, especially when the diverticulum is on the side or at the inferolateral angle, and it permits its extravesical removal without opening the bladder. A pararectus incision is made from the umbilicus to 2.5 cm. above Poupart's ligament and is then continued at a right angle to the midline. This gives much more room than through the standard midline incision, permits sharp dissection if there is peridiverticulitis and facilitates identification and isolation of the ureter several inches above the diverticulum.

The bladder is not opened in the midline as in the usual combined extravesical and intravesical method. The diverticulum is freed by blunt and sharp dissection and is severed from the bladder. The opening is then closed from the outside after a tube is inserted through it for drainage. This does away with another artificial opening into the bladder. It is, of course, imperative to remove whatever obstruction may exist at the vesical neck before excision of the diverticulum is planned. This can usually be done transurethrally. The advantages and disadvantages of the various methods of diverticulectomy are discussed.

Kutzmann [32] stated that diverticulum of the urinary bladder of the female occurs rarely. This lesion is the result of both congenital and acquired anatomic factors. Diverticula form less frequently in women since there are fewer acquired obstructive factors of sufficient severity.

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31. Melen, D. R.: Lateral Approach for Operating upon Diverticula of the Bladder, Surg., Gynec. & Obst. **61**:184 (Aug.) 1935.

32. Kutzmann, A. A.: Diverticulum of the Urinary Bladder in Women, Am. J. Surg. **29**:102 (July) 1935.

These acquired factors, as demonstrated in his cases, are contracture of the neck of the bladder, stricture of the urethra, caruncle, hypertrophy of the trigon and polyps at the neck of the bladder. Clinically, diverticulum of the bladder of the female has no pathognomonic syndrome. It is a disease of old age. The symptoms in most cases are those of infection of the urinary tract plus obstruction. In the majority of his cases difficulty in urination did not prove to be a significant symptom, as with men. The duration of the condition over a long period of years seems to be the only significant clinical fact. Differential diagnosis is to be made from false or incipient diverticulosis, a perivesical abscess with rupture into the bladder, a patent urachus or hydro-urachus, a fistulous opening to an intestinal carcinoma, hernia of the bladder or an hour-glass bladder. Treatment in most cases was directed to the causative obstructive condition.

Cystitis Follicularis.—Hinman and Cordonnier [33] reported 7 cases which presented cystoscopically the picture of cystitis follicularis. The diagnosis was confirmed by biopsy in 5 cases in the series. Cystoscopy reveals that the mucosa is studded with discrete nodules of varying size, averaging about 2 mm. in diameter. In some areas, particularly over the trigon and base of the bladder, the nodules are so closely packed that they appear confluent and resemble Peyer's patches in the intestine. Each nodule has a solid appearance in contrast to the more translucent character of the cysts in cases of cystitis cystica. There is a generalized capillary injection of the mucous membrane, such as is observed in cases of chronic cystitis. Microscopically, each nodule is composed of a solitary lymph follicle with densely packed lymphocytes at the periphery and a typical germinal center. Clinically, there are no distinguishing symptoms. They are those of chronic inflammation of the bladder. At times the patient is entirely without symptoms, and still the mucosa of the bladder is found to be covered with these nodules. All of the patients in this series had recurrent attacks of dysuria, such as frequency, burning, urgency and nocturia. Cystitis follicularis must be differentiated from cystitis cystica, cystitis glandularis, cystitis granulosa, cystitis emphysematosa and bullous edema.

Ulcer.—Lazarus [34] stated that simple chronic ulcer of the urinary bladder is a distinct clinical entity, the etiology of which is unknown. The lesion, while usually solitary, may occur in more than one place. The site of predilection is the trigon, particularly the region about the orifices of the ureters. The significant symptoms are dysuria, fre-

33. Hinman, Frank, and Cordonnier, Justin: Cystitis Follicularis, J. Urol. **34**:302 (Oct.) 1935.

34. Lazarus, J. A.: Simple Chronic Ulcers of the Urinary Bladder. Report of an Unusual Case, J. Urol. **34**:111 (Aug.) 1935.

quency and hematuria. The kidneys are never affected. Calcification occurs in a later stage of the life cycle of this ulcer; so when one is seen early encrustation is not present. Generally, the capacity of the bladder is not reduced. The diagnosis is made by excluding any of the usual causes of ulcer of the bladder such as tuberculosis, syphilis and neoplasm. The prognosis in cases of simple chronic ulcer is favorable. Treatment has consisted of the application of silver nitrate, scraping of the ulcers or excision. Lazarus did not obtain satisfactory results with these methods but did obtain a complete cure by the intravenous injection of neoarsphenamine.

Bilharziasis.—Loeweneck,[35] in discussing schistosomiasis, stated that cystoscopy in cases of bilharziasis furnishes the most data if performed a few days after treatment has been instituted. The Morgenstern cystoscope is the most satisfactory instrument to use in examining, checking and treating this condition. Simple urinalysis is of small value in determining whether the condition is still present; cystoscopic examination is usually necessary. The disappearance of eosinophilia is the most decisive evidence of a cure.

Vesicovaginal Fistula.—Lower [36] stated that vesicovaginal fistula is regarded as an extremely rare condition but that in spite of improved surgical and obstetric technic there is still a considerable number of women who present themselves for treatment of this lesion. It may result following childbirth or from a surgical accident during a pelvic operation, or it may result from a malignant condition of the bladder or cervix, from the application of radium in the treatment of a malignant process in the pelvis or from the invasion of the malignant growth itself. Fistula developed in a series of 71 cases reported by Lower as follows: as a result of childbirth in 10 cases in which cancer was not present and as a result of operative trauma in 32; and in cases in which cancer was present, as a result of operative trauma in 11, radium treatment in 13 and invasion by cancer which had not been treated in 5.

Treatment of this lesion must be individualized, for no one type of operation or approach can be used satisfactorily in all cases. In many of the cases observed by Lower repeated unsuccessful attempts have been made to close the fistula. In 1 case an attempt at repair had been made eleven times. Each effort at treatment is made more difficult by the presence around the opening of hard, fixed scar tissue. The choice of the method in treating this condition depends on the

35. Loeweneck, M.: Zur Behandlung der Schistosomiasis haematobium, Ztschr. f. urol. Chir. **40**:202, 1934.

36. Lower, W. E.: The Treatment of Vesicovaginal and Ureterovaginal Fistula, Am. J. Surg. **28**:234 (May) 1935.

position of the opening, its size, the amount of cicatricial tissue that surrounds it and whether or not malignant disease is present. The following types of operations were used in this series of cases: repair of the fistula by the transvesical approach (8 cases) and by the vaginal approach (28), ureteral transplantation into the intestines (10) and into the bladder (3) and nephrectomy (3). There was no treatment in 19 cases.

Cullen [37] stated that when a vesicovaginal fistula is high and the vagina narrow, closure may be difficult. If Schuchardt's incision is made, the fistula comes clearly into view and may be more readily closed. If sufficient exposure cannot be obtained by one incision of this type, it may be necessary to make a similar one on the opposite side of the vagina. In rare cases in which the greater part of the base of the bladder is missing and in which one orifice of the ureter opens on the margin of the fistula, it may be difficult to make a satisfactory closure of the fistula. Free mobilization of the bladder is essential. Owing to the fact that the ureter runs obliquely in the wall of the bladder for more than 1 cm., it can be slit at least 1 cm. Its opening into the bladder is then well removed from the edge of the fistula, which can be satisfactorily closed. Fistula following complete hysterectomy for cancer of the cervix formerly occurred rather frequently. After removing the uterus, Cullen sutures the peritoneum of the bladder to the cut edge of the anterior wall of the vagina. After this procedure, when the bladder distends it is only the peritoneally covered portion that dilates. The base of the bladder, where fistula is prone to develop, remains contracted and is well protected. In Cullen's cases the number of postoperative fistulas has been markedly decreased by this simple method. In many complicated cases of myoma it has been necessary to dissect out one or both ureters to ascertain whether they have been injured, at which time any damage can be immediately corrected.

Miller [38] stated that the popularity of transplantation of the ureters may tend to do away with more conservative measures in the management of vesicovaginal fistulas. The success of closure of this lesion depends on wide separation of the bladder and vaginal wall and independent closure of these two layers. In some cases in which the fistula is unusually large, the bladder has been closed without any attempt to coapt the vaginal area. If there is extensive destruction, separation of the two layers should be sufficiently wide to permit closure of the lesion of the bladder without tension; no sutures should be placed in

37. Cullen, T. S.: Discussion on Vesicovaginal Fistula, Am. J. Surg. **28**: 265 (May) 1935.

38. Miller, C. J.: Discussion on Vesicovaginal Fistula, Am. J. Surg. **28**:269 (May) 1935.

the vaginal layer. Another feature is to separate the uterus from the bladder, even to the extent of opening the peritoneal sac, making a wide separation of the bladder from the broad ligaments above. This facilitates closure of extensive lesions with satisfactory results.

Atony.—Braasch and Thompson [39] stated that atony of the bladder is never primary; it is caused by abnormal innervation, by obstruction or by both. Continuous retention of urine from any cause will produce atony of the vesical wall. In some cases it may be difficult to determine which factor is involved. In most cases of atony, obstruction, either primary or secondary, is the predominating factor. The factors involving sphincteric dysfunction are imbalance of innervation, with predominance of the sympathetic or filling nerves; rigidity, or failure of adequate relaxation of the internal sphincter, referred to as "dysectasia," and apparent failure of coordination of reflexes involved in the act of urination centering in the vesical neck, to which the term achalasia has been given. The first condition can be favorably influenced by presacral neurectomy, and the second usually can be remedied by thorough transurethral resection. The abnormal tissue, which interferes with the function of the neck of the bladder, may in some cases be overlooked. It is necessary to remove such tissues completely and to free every cicatricial contraction in order to restore sphincteric function. Sphincteric abnormality in the female presents problems quite different from those offered by corresponding conditions in the male. In most cases judicious removal of sphincteric tissue will overcome retention, but subsequent presacral neurectomy may be necessary. Localized or partial atony may follow destruction of branches of the pelvic nerves in the course of an operation on the bladder. Various other types of atony may occur.

With acute retention, such as frequently occurs following an abdominal operation, the advisability of drainage of the bladder before it becomes overdistended should be emphasized. In contrast, with retention following extensive injury to the spine, overflow of the bladder should be permitted rather than catheterization.

Musculature of Vesical Neck.—Macalpine [40] stated that two muscles, one voluntary and the other involuntary, and an inch or more apart, exist at the neck of the bladder, both functioning as sphincters. This dual musculature is explained by the emergence of the ejaculatory ducts between them. If both of these muscles are open when semen is discharged, secretion may escape into the bladder or to the exterior; also any urine in the bladder will flow out. The internal sphincter

39. Braasch, W. F., and Thompson, G. J.: Treatment of the Atonic Bladder, Surg., Gynec. & Obst. **61**:379 (Sept.) 1935.

40. Macalpine, J. B.: The Musculature of the Bladder Neck of the Male in Health and Disease, Proc. Roy. Soc. Med. (Sect. Urol.) **28**:39 (Nov.) 1934.

is usually tightly contracted during ejaculation. Instances are cited in which the internal sphincter is paralyzed or injured after operation in cases of prostatic hypertrophy and of certain nervous diseases. Two cases are reported of direct injury to this localized region, with the result in all cases that ejaculation failed. In cases of hypertrophy of the prostate gland the internal sphincter is dilated by the growing adenoma, and at operation it is further stretched and perhaps cut across. Continence then depends on the external sphincter. Two cases are reported in which the external sphincter had previously been paralyzed, total incontinence resulting.

In disease of the central nervous system dilatation of the internal sphincter resulting in funnel-neck is common. A series of patients with disease of the nervous system were examined in order to determine the frequency of this sign. Other cases were reported in which it occurred independent of any nervous condition.

The part the sphincters play in ejaculation is discussed and illustrated by reports of further cases of paralysis of the sphincters. In the normal way the external sphincter weakens during coitus, especially during ejaculation, but when the internal sphincter is paralyzed no weakening is evident. Penile erection is associated with spasm of the internal sphincter, and spasm of the internal sphincter produced by irritation, such as stone in the bladder, may produce priapism. The varying types of adenoma bear different relationships to the internal sphincter. The view that submucosal glands give rise to enlargement of the prostate is supported. The influence of enlargement of this gland on the internal sphincter is discussed.

Cystometry.—Watts and Uhle [41] presented evidence of representation of the bladder in the cerebral cortex and the region of the hypothalamus and even more caudal in the brain stem. The nature of the evidence indicated that representation for this viscus contains both excitatory and inhibitory units. Eleven patients with tumor of the brain associated with neurogenic bladder were studied. Patients with hypertonic curves gave histories of urgency and periodic involuntary urination. Two patients with hypotonic curves had difficult urination, followed by retention requiring catheterization. The other patients with this type of curve had no urinary symptoms. The abnormalities of function, tone and sensation of the bladder of patients with tumor of the brain are probably the result of a disturbance of representation of the bladder in certain parts of the brain or of tracts descending from them.

41. Watts, J. W., and Uhle, C. A. W.: Bladder Dysfunction in Cases of Brain Tumor: A Cystometric Study, J. Urol. **34**:10 (July) 1935.

TESTES

Tumor.—Hinman and Powell [42] stated that tumor of the pituitary gland, embryonal tumor and pregnancy are known causes of the appearance in the urine of gonad-stimulating hormones. The stimulation of growth of the gonads and genitals of infantile animals varies with the origin of the hormone producing it, the amount present in the urine and the animal used for the injections. Infantile mice and rats are used. A qualitative test for as low as 250 units is made first on fresh, unaltered morning urine. If the reaction is positive, a quantitative test can be made. The microscopic ripening of graafian follicles is more easily observed in mice than in rats, and the gross enlargement of the uterine horns is more definite and diagnostic in mice than in rats.

The majority of tumors of the testes are embryonal, and the urine of patients with such a tumor contains a substance which produces gross enlargement of the uterine horns or microscopic ripening of ovarian follicles when injected into infantile female mice and rats. The presence of such a gonadotropic hormone in the urine of a patient with a tumor of the testis is presumptive evidence of malignancy of the testis, and its absence is strong but not definite evidence against the presence of a malignant condition. The effect of irradiation on the amount of hormone in the urine, as determined by quantitative methods before and after irradiation, gives a good indication of radiosensitivity, and it may be used as a therapeutic test in conjunction with the clinical effect on metastasis, when present. The therapeutic test of irradiation must be interpreted in conjunction with the histologic structure of the tumor, the clinical absence of metastasis or the character of metastasis when present and the physical condition of the patient. The hormonal test, correlated as before mentioned, permits more accurate prognosis and better control of treatment than has been possible heretofore, and it may be of value in the classification of tumors the nature of which is questionable on histologic study alone.

Hinman [43] stated that the prognosis and treatment of a tumor of the testis may be determined by the following three considerations and lines of procedure. Early and definite diagnosis is the first step in the treatment of the disease. The hormonal test, in the short period of its application, seems to indicate with accuracy the presence or absence of a testicular malignant process. The second step is the determination of the presence or absence of metastasis by clinical examination and biologic test. For practical purposes, patients can be divided into two groups: those without metastasis and those with metastasis. The

42. Hinman, Frank, and Powell, T. O.: The Gonadotropic Hormone in the Urine of Men with Tumor of the Testis, J. Urol. **34**:55 (July) 1935.

43. Hinman, Frank: The Prognosis and Treatment of Tumors of the Testis, J. Urol. **34**:72 (July) 1935.

advantage of the hormonal test in the control of treatment is shown in Hinman's cases. Patients who do not have metastasis fail to excrete the hormone within two weeks after castration. When the hormone persists, though reduced in quantity, metastasis has probably occurred even though it cannot be demonstrated clinically. The third step is the consideration of radiosensitivity. This can be predicted by past experience with similar tumors and clinically tested by watching the effect of irradiation on metastasis, when present, and on the amount of hormone in the urine. The determination of this sensitivity may be called the therapeutic test of irradiation. From 3,000 to 4,000 roentgen units to each field, requiring a period of three weeks for administration, will show by the effect clinically on metastasis, and biologically on the amount of hormone excreted one to two weeks later, the relative degree of radiosensitivity.

On the basis of the foregoing considerations patients may be divided into two groups: Group 1 contains those patients without clinical evidence of metastasis who are in good physical condition; these can be subdivided, by the result of a hormonal test two weeks after castration, into a negative and a positive subgroup. The negative subgroup includes the few patients cured by castration. All of these patients should, however, receive a hormonal test every three to six months for two years or longer. Reappearance of the hormone in the urine indicates metastasis. Should the microscopic structure of the tumor be similar to that which experience has shown is highly radioresistant, early radical removal of the preaortic lymph zone should be considered, regardless of the effect of castration on the hormone. The disappearance of the hormone after castration is only relative evidence of cure, for metastasis may not produce sufficient hormone in the urine to give a reaction. Group 2 contains patients with clinical evidence of metastasis. Castration may be indicated for local relief but is done mainly for diagnosis. Experience has shown that these patients are inoperable and that irradiation is the only curative treatment. The prognosis depends on the extent and rapidity of metastasis and the general physical condition of the patient as well as on the type of tumor and its radiosensitivity.

A fairly accurate forecast of the probable course in any given case is possible by these studies. The chance of recovery may be estimated as good, fair or poor. The prognosis is good when the patient is physically fit, there is no demonstrable metastasis and the hormone has disappeared from the urine. The patient's condition is considered as fair when he is in good physical condition and the structure of the tumor indicates that it will respond well to roentgen therapy; however, metastasis has appeared, and the hormone has persisted, even though it appeared to be diminishing under irradiation. A poor outcome is

expected when the patient loses ground physically, when metastasis resists treatment or recurs rapidly and when the amount of hormone in the urine is only slightly affected or even increases.

Of 25 patients with no evidence of metastasis, 14 underwent radical operation, 9 for tumor on the right side and 5 for tumor on the left side. Ten were living at the time of the report, all with a good prognosis; 4 were dead. Seven showed metastasis in the glands removed at operation; 4 of these patients were living, after fourteen years, four years and ten months, one year and one month, and three months, respectively. Three are dead. Seven had glands removed which did not show metastasis; in 2 of these patients there was an unusual degree of endothelial hyperplasia, and 1 was living and well after six years and one month and the other was dead. The 5 remaining patients were still living, after eight years and nine months, two years and eight months, one year and four months and one year (2), respectively.

Of the 11 patients without metastasis treated by castration and roentgen rays, 8 were living: 1 after two years, with a good prognosis; 4 with only a fair result because the hormonal tests gave positive results, and 3 with a definitely poor prognosis. Of the 4 patients with a fair prognosis, 1 lived seven years before metastasis appeared, but the amount of hormone in the urine was increasing in spite of roentgen therapy; another lived seven years since castration, but although metastasis was not evident clinically, the amount of the hormone in the urine was increasing, and the other 2, with a fair prognosis, had lived one and three years, respectively, without clinical evidence of metastasis but with positive reactions to hormonal tests. Of 29 patients with clinical evidence of metastasis when first seen, only 10 were alive, 4 with a fair prognosis.

Infection.—Mathé [44] reported a case of the fulminating type of testicular abscess, due to the colon bacillus, affecting a young man with nongonorrheal infection of the genito-urinary tract. It followed instrumentation; a differential diagnosis was difficult to make, and the condition was relieved by orchidectomy.

Suppurative orchitis is relatively infrequent compared to epididymitis, epididymo-orchitis and orchitis, but it is not a rare disease. The possibility of its presence should be considered when acute inflammatory processes of the testis are being dealt with. Infection of the testis takes place through the blood stream, lymph channels and natural channels by way of the vas deferens and may be due to torsion of the spermatic cord, to trauma to the testis during operation or to toxic poisoning. It is a complication of gonorrheal and nongonorrheal urethritis; it may follow catheterization or operation on the prostate

44. Mathé, C. P.: Suppurative Orchitis: Its Diagnosis and Treatment, J. Urol. **34**:324 (Oct.) 1935.

gland when infection is present, and it occurs in cases of infections of the genito-urinary system in general. The important facts in the diagnosis of suppurative orchitis are persistent fever, leukocytosis, progressive swelling, pain and tenderness of the testis and local fluctuation. Early diagnosis of abscess of the testis makes possible the saving of testicular tissue by prompt incision and drainage.

Rosenberg [45] reported 6 cases of abscess of the testis and 1 case of necrosis of the testis. Four of the abscesses were associated with gonorrhea and a complicating epididymitis; in 2 cases the condition was due to chronic infection of the urinary tract by nonspecific epididymitis. The necrosis was probably due to torsion of the spermatic cord following violent muscular effort. Abscess of this organ is usually due to some infection either in the urinary or in the genital tract, excluding instances in which it is associated with typhoid, influenza, cellulitis and osteomyelitis. In the last-named condition, involvement of the testis is probably of hematogenous origin.

Generally there are four types of abscess of the testis. Abscesses associated with gonorrhea and a complicating epididymitis are usually small, and the testis generally sloughs out in its entirety. Abscesses associated with chronic infection of the urinary tract or genital tract are usually large and cause complete destruction of the testis. They occur in such conditions as obstruction of the prostate gland when drainage by a catheter has been instituted and urethral instrumentation has been employed. The third type is associated with torsion of the spermatic cord. The fourth type is associated with systemic infections, such as typhoid, variola, influenza and cellulitis, and is usually a true orchitis and rarely leads to suppuration. When testicular abscesses occur in this instance, they are probably due to phlebitis of the spermatic vessels. Abscess of the testis associated with tuberculosis or a malignant condition is not considered. Abscess of the testis usually results in complete destruction of the organ, whether or not drainage is instituted. Early diagnosis is essential in order to conserve as much testicular tissue as possible.

Undescended Testis.—Webster,[46] who treated 11 patients who had undescended testes with an extract of the urine of pregnant women, stated that in 10 of the cases the testes descended into the scrotum during treatment. The 1 case in which failure occurred was that of a man 26 years of age who had undergone previous exploration of the inguinal canal, the purpose being to locate the organ. In all of 3 cases of bilateral undescended testis, descent into the scrotum occurred. In 2

45. Rosenberg, William: Abscess of the Testicle, J. Urol. **34**:44 (July) 1935.

46. Webster, Bruce: Effect of Anterior Pituitary-Like Principle from the Urine of Pregnancy on Undescended Testes in Man, J. A. M. A. **104**:2157 (June 15) 1935.

instances hernias persisted three months after descent of the testes. Through these hernias the testes could be pushed back into the inguinal canal. In each instance the testes tended to increase in size after their descent into the scrotum, and in 3 cases the affected organ could not be differentiated from the normal one on physical examination three months after cessation of treatment. The others remained smaller than normal. All of them increased in degree of firmness. Assays of the urine of the 5 boys who were above the age of 11 years for testes hormone showed no definite change after treatment. This was expected since all of the patients except 1 had normal secondary sexual characteristics, and in this instance the departure from normal was not extreme.

The dosage of the extract of the urine of pregnant women was more than that used in most of the other cases previously reported. No reactions were encountered except slight erythema at the site of the injection. With this system of dosage, descent of the testis usually occurred during the third week of treatment. The period during which the hormone is administered as well as the total number of units given is a factor. Although these cases were unselected, it is probable that there was an element of chance in determining the high percentage of cases in which descent occurred, since it is likely that in a certain group of cases the testes are prevented from descending by mechanical block, such as that caused by the adhesions commonly found at operation. No conclusions could be made in regard to the mechanism that was responsible for the descent of the testes.

PENIS

Preputial Stone.—Ingraham [47] stated that preputial stone occurs in those cases of phimosis, usually congenital, in which the orifice for the passage of urine becomes so small that stagnation occurs in the preputial sac, which is distended by pressure of urine from the bladder. The anterior portion of the urethra becomes dilated, and the bladder hypertrophies and enlarges. Hydro-ureter may develop if the condition continues over a long period. In the presence of infection, the débris from which forms a nucleus, stagnation of urine is likely to result in the deposit of urinary salts to form calculi in the kidneys, bladder or preputial sac. The calculi formed high in the urinary tract are caught by the phimosed prepuce if they are carried downward by the flow of urine, and the result is the same as though they were formed in the latter situation. The stones consist of organic matter impregnated with calcium or magnesium phosphate or urate, occasionally of ammonium salt or uric acid. They increase more or less rapidly in size as successive

47. Ingraham, N. R., Jr.: Preputial Calculus, a Clinical Rarity: Report of a Case, J. A. M. A. **105**:106 (July 13) 1935.

layers are deposited. If the condition is not treated, obstruction of urine of severe degree will develop, which without intervention may give rise to the formation of a fistula. Chronic irritation has caused the development of cancer of the glans penis in at least one instance, and pressure atrophy of the glans is common. Diagnosis rests on the realization of the existence of such a condition, and the treatment, without exception, is circumcision.

Tumor of Cowper's Gland.—Uhle and Archer [48] stated that primary carcinoma of Cowper's gland is exceedingly rare. Only 4 cases were found in the literature of the various countries of the world. The etiology of this lesion is obscure. Uhle and Archer reported a case in which they considered themselves warranted in identifying the tissue as adenocarcinoma arising primarily from Cowper's gland. The alveolar spaces were numerous and were lined with small cells of pyriform type in which mucous-secreting elements were evident. Hyperplasia of the intra-acinar type was definite. These hyperplastic acini showed wide variation in size; in some areas the acini were represented by small islands of epithelial cells with no definite arrangement and appeared to lack a basement membrane.

Symptoms in cases of malignancy of Cowper's gland are primarily in the perineum and rectum. Persistent local discomfort, aggravated by sitting or walking, and pain on defecation are the most common symptoms. If frequency, urgency, dysuria and burning are also present, the lesion has probably extended to the urethra or periurethral tissue. If urinary difficulties are the predominating symptoms, the diagnosis of primary carcinoma of the urethra is more probable. Sometimes the chief complaint is that of a lump or swelling in front of the anus. Tenderness may or may not be present. The skin of the perineum may or may not be fixed. The proximity of the neoplasm to the rectal wall often leads to a mistaken diagnosis of a rectal lesion. The patient in the case herein reported was treated for an anal fistula; the mucosa of the rectum was fixed to the mass, while the boundaries of the infiltrative tissue were difficult to discern both by perineal and by rectal examination.

The treatment of carcinoma of Cowper's gland is surgical. Early diagnoses have been rare; most patients have been seen in the end-stages, when only a portion of the tumor could be excised, so that a remnant had to be left to be treated by palliative measures. With the addition of roentgen and radium therapy, more satisfactory results may be expected in the future.

48. Uhle, C. A. W., and Archer, G. F.: Primary Carcinoma of Cowper's Gland: Report of a Case with a Review of the Literature, J. Urol. **34**:128 (Aug.) 1935.

(To be Concluded)

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